ENANTIOSELECTIVE INTRAMOLECULAR AZA-SPIROANNULATION ONTO BENZOFURANS USING CHIRAL RHODIUM CATALYSIS

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Supporting Information

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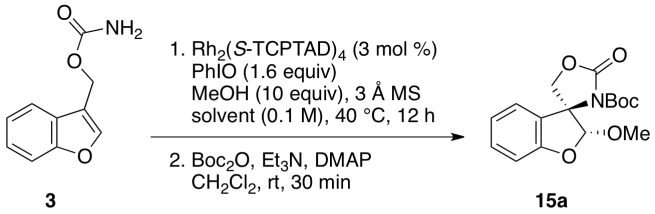
General Experimental Procedures:

All reactions were stirred magnetically, under an atmosphere of argon, unless otherwise specified. Reactions were monitored by thin-layer chromatography (TLC) carried out on silica gel plates (Merck silica Kieselgel 60 F_{254}). Flash column chromatography was performed on silica gel 60N (Kanto Chemical Co., Inc., spherical, neutral, 40-50 μm) or CHROMATOREX® (FUJI SILYSIA CHEMICAL Ltd., SO3H MB100-40/75). Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on JEOL JNM-AL400 (400 MHz), JEOL ECP500 (500 MHz), and JEOL JNM-ECA600 (600 MHz) spectrometers. Chemical shifts (δ) are given in parts per million (ppm) relative to internal TMS (0.00 ppm) in $CDCl_3$ or residual non-deuterated solvent peak (DMSO-d_6: 2.49 ppm, CD_3OD: 3.30 ppm) as internal standard. Coupling constants (*J*) are reported in Hz. The following abbreviations are used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br s, broad singlet; br d, broad doublet; dd, double doublet; ddd, double double doublet; dddd, double double double doublet; dq, double quartet; ddt, double double triplet; tt, triple triplet. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded on JEOL JNM-AL400 (100 MHz), JEOL ECP500 (125 MHz), and JEOL JNM-ECA600 (150 MHz) spectrometers. Chemical shifts are given in ppm relative to the center line of the triplet of $CDCl_3$ (77.0 ppm), the center line of the septet of DMSO-d_6 (39.7 ppm), or the center line of the septet of CD_3OD (49.0 ppm). Optical rotations were measured on JASCO P-2200 Digital Polarimeter at rt, using the sodium D line. Infrared spectra were recorded on a JASCO *FT/IR*-410 Fourier Transform Infrared Spectrometer. Mass spectra were recorded on JMS-DX303, JMS-700 or JMS-T 100 GC using electron impact (EI) or fast atom bombardment (FAB). HPLC utilized Gilson Model 307 or Gilson Model 305 with Gilson Model 112 or Gilson Model 119 as UV-detector (254 nm). Analytical chiral HPLC was performed on CHIRALCEL OD-H, CHIRALPAK AD-H, CHIRALPAK IC, and CHIRALPAK IA (each is 4.6 mm x 25 cm) obtained from Daicel Chemical Industries, ltd.

Screening of reaction conditions.

Table S1: Screening of solvents.



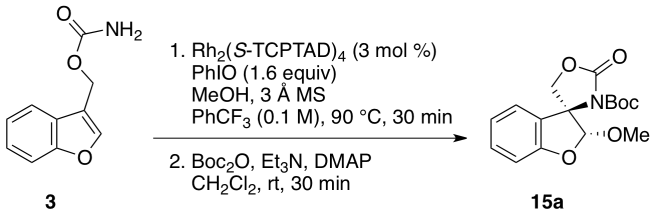
3 **15a**

entry	solvent	yield[a] / ee[b]
1	CH_2Cl_2	45% / 20% ee
2[c]	MeOH	28% / 22% ee
3	AcOEt	48% / 27% ee
4	PhH	32% / 55% ee
5	$PhCF_3$	54% / 70% ee
6	PhF	57% / 67% ee
7	PhCl	45% / 66% ee
8	$PhNO_2$	38% / 66% ee

[a] Isolated yield. [b] Enantiomeric excess was determined by chiral HPLC analysis.

[c] MeOH was used as a solvent instead of the additive.

Table S2: Screening of the amount of MeOH.

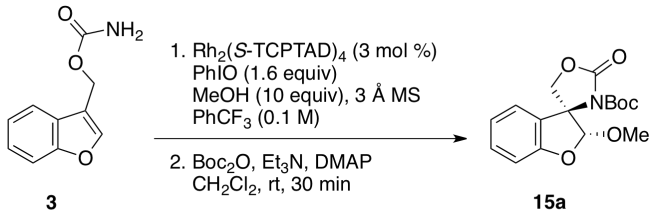


3 **15a**

entry	MeOH	yield[a] / ee[b]
1	2 equiv	13% / 48% ee
2	5 equiv	26% / 58% ee
3	10 equiv	53% / 68% ee
4	20 equiv	60% / 62% ee
5	50 equiv	52% / 55% ee

[a] Isolated yield. [b] Enantiomeric excess was determined by chiral HPLC analysis.

Table S3: Screening of the reaction temperature.



3 **15a**

entry	temperature	time	yield[a] / ee[b]
1	90 °C	30 min	53% / 68% ee
2	40 °C	12 h	54% / 70% ee
3	rt	16 h	52% / 79% ee
4	0 °C	16 h	69% / 86% ee
5[c]	−23 °C	16 h	0% / -

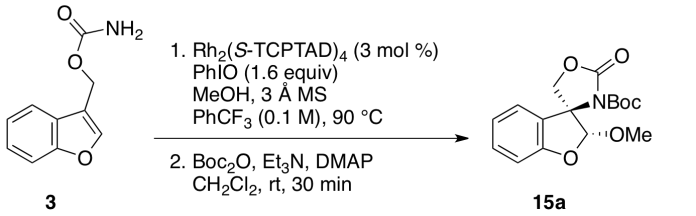
[a] Isolated yield. [b] Enantiomeric excess was determined by chiral HPLC analysis.

[c] No reaction.

Additional experimental results

Enantiomeric excess of the spirocycle **15a** was checked at low product conversion (5 min) in the course of optimization of reaction conditions. Rh_2(*S*-TCPTAD)$_4$ (cat.)/PhIO/MeOH/3 Å MS/PhCF3/90 °C systems, not optimized reaction conditions, were adopted at that time. As the result, the same level of ee was observed (**Scheme S1**).

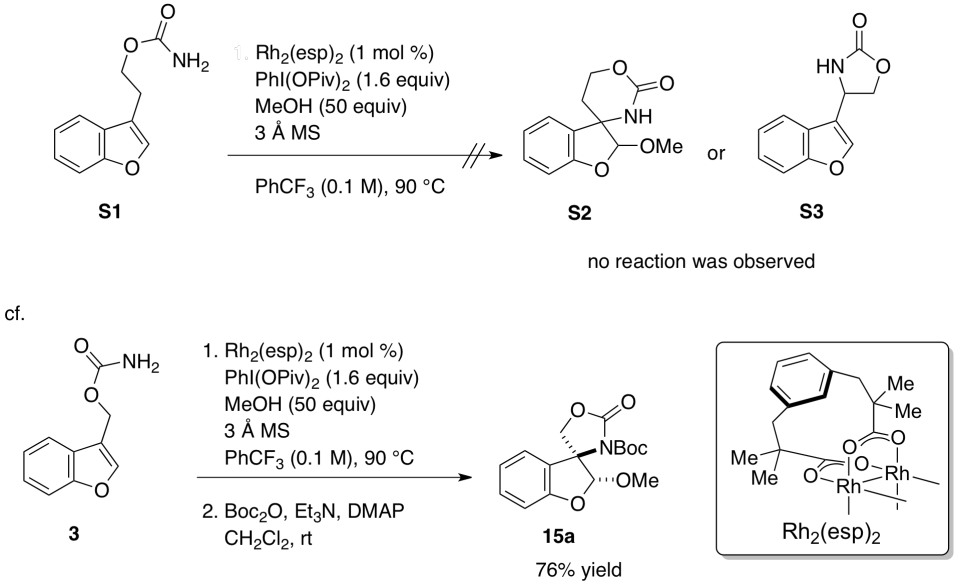
Scheme S1: Enantiomeric excess at low product conversion



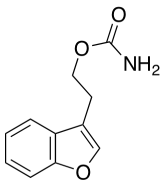
[a] Enantiomeric excess was determined by chiral HPLC analysis.

The C2 analogue of benzofuran **3** was synthesized, and subjected to the aza-spiroannulation conditions with $Rh_2(esp)_2$ [1] ($Rh_2(esp)_2$ is an achiral Rh(II) complex which usually indicates high reactivity). However, no reaction was observed: neither the spirocycle **S2** nor the C-H insertion product **S3** was obtained (**Scheme S2**).

Scheme S2: The C2 analogue of benzofuran 3



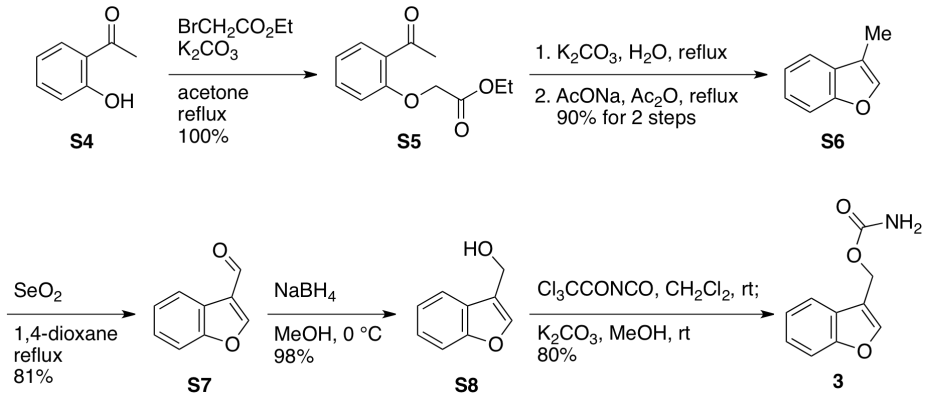
Carbamic acid 2-benzofuran-3-yl-ethyl ester (S1)



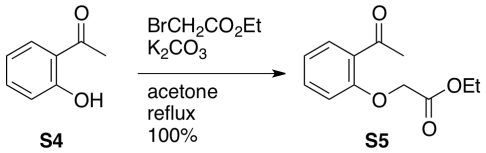
^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.57 (1H, d, *J* = 7.5 Hz), 7.48 (1H, s), 7.47 (1H, d, *J* = 9.0 Hz), 7.31-7.27 (1H, m), 7.26-7.21 (1H, m), 4.82 (2H, br s), 4.35 (2H, t, *J* = 6.6 Hz), 3.01 (2H, t, *J* = 6.6 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 156.8, 155.2, 141.9, 127.9, 124.3, 122.4, 119.4, 116.4, 111.5, 64.0, 23.6. IR (neat, cm^{-1}): 3417, 3330, 3260, 3210, 1685, 1616. MS *m/z*: 205 (M^+), 144 (100%). HRMS (EI): Calcd. for $C_{11}H_{11}NO_3$: 205.0739, found: 205.0737.

Preparation of substrates for aza-spiroannlation reactions

Scheme S3: Preparation of benzofuran 3.



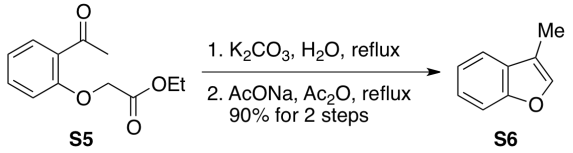
cf. Synthesis of **S7** from **S4**: ref. (2). Installation of a carbamate moiety (**S8** → **3**), see: ref. (3) and (4).



(2-Acetyl-phenoxy)-acetic acid ethyl ester (**S5**)[2,5]: A mixture of 2-acetylphenol **S4** (50.0 g, 367 mmol), ethyl bromoacetate (49 mL, 441 mmol) and K_2CO_3 (102 g, 738 mmol) in acetone (367 mL) was refluxed for 17 h. After cooling, the mixture was quenched with addition of aqueous HCl, and the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:2 AcOEt:Hexane) to give ester **S5** (81.3 g, 366 mmol, 100%) as a

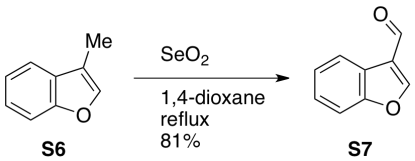
colorless solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.77 (1H, dd, *J* = 7.6, 1.6 Hz), 7.48-7.41 (1H, m), 7.06 (1H, dd, *J* = 7.6, 7.6 Hz), 6.83 (1H, d, *J* = 8.2 Hz), 4.73 (2H, s), 4.28 (2H, q, *J* = 7.1 Hz), 2.72 (3H, s), 1.31 (3H, t, *J* = 7.1 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 199.6, 168.1, 156.9, 133.4, 130.6, 128.7, 121.6, 112.1, 65.4, 61.4, 31.9, 14.0. IR (neat, cm^{-1}): 2978, 2930, 1757, 1668, 1596. MS *m/z*: 222 (M^+), 149 (100%). HRMS (EI): Calcd. for $C_{12}H_{14}O_4$: 222.0892, found: 222.0892.



3-Methylbenzofuran (**S6**)[6]: Into the vigorously stirred solution of K_2CO_3 (76.0 g, 549 mmol) in water (610 mL) was added ester **S5** (81.3 g, 366 mmol), and the mixture was gently refluxed for 12 h. After the reaction mixture was cooled to 0 °C, the mixture was carefully acidified with aqueous HCl. The deposited precipitate was filtered off, washed several times with cold water to provide (2-acetyl-phenoxy)-acetic acid that was carried on without further purification. A mixture of crude (2-acetyl-phenoxy)-acetic acid and anhydrous AcONa (120 g, 1.46 mol) in Ac_2O (242 mL) was refluxed for 13 h. After cooling, water was added, and the resultant solution was extracted with Et_2O. The combined extracts were washed with saturated aqueous Na_2CO_3 solution, with water, and then with brine, and finally dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hexane) to give benzofuran **S6** (43.7 g, 331 mmol, 90% for 2 steps) as a colorless oil.

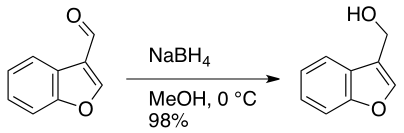
^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.55 (1H, d, *J* = 7.3 Hz), 7.47 (1H, d, *J* = 7.8 Hz), 7.42 (1H, d, *J* = 1.0 Hz), 7.34-7.23 (2H, m), 2.27 (3H, d, *J* = 1.0 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 155.3, 141.3, 129.0, 124.0, 122.2, 119.4, 115.6, 111.3, 7.9. IR (neat, cm^{-1}): 3063, 2923, 1589. MS *m/z*: 132 (M^+), 132 (100%). HRMS (EI): Calcd. for C_9H_8O: 132.0575, found: 132.0583.



Benzofuran-3-carbaldehyde (**S7**)[2]: A mixture of benzofuran **S6** (5.00 g, 37.8 mmol) and SeO_2 (10.5 g, 94.6 mmol) in dry 1,4-dioxane (38 mL) was refluxed for 22 h. The resulting black precipitate was filtered off and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:8 AcOEt:Hexane) to give aldehyde **S7** (4.47 g, 30.6 mmol, 81%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 10.18 (1H, s), 8.27 (1H, s), 8.21-8.17 (1H, m), 7.58-7.54 (1H, m),

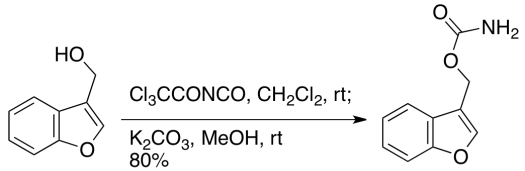
7.45-7.37 (2H, m). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 184.7, 156.0, 155.2, 126.3, 124.9, 123.7, 122.9, 122.6, 111.7. IR (neat, cm^{-1}): 3134, 3087, 2826, 2743, 1684, 1556. MS *m/z*: 146 (M^+), 146 (100%). HRMS (EI): Calcd. for $C_9H_6O_2$: 146.0368, found: 146.0389.



S7 **S8**

Benzofuran-3-ylmethanol (**S8**): To a solution of aldehyde **S7** (2.50 g, 17.1 mmol) in MeOH (43 mL) was added $NaBH_4$ (971 mg, 25.7 mmol) at 0 °C, and the mixture was stirred for 1 h. The reaction mixture was added saturated aqueous NH_4Cl, and MeOH was evaporated under reduced pressure. The resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:2 AcOEt:Hexane) to give alcohol **S8** (2.49 g, 16.8 mmol, 98%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.69-7.66 (1H, m), 7.62 (1H, s), 7.49 (1H, d, *J* = 8.2 Hz), 7.34-7.30 (1H, m), 7.29-7.25 (1H, m), 4.85 (2H, d, *J* = 5.5 Hz), 1.60 (1H, t, *J* = 5.5 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 155.4, 142.2, 126.6, 124.4, 122.6, 120.2, 119.8, 111.4, 55.4. IR (neat, cm^{-1}): 3342, 2936, 2876, 1581. MS *m/z*: 148 (M^+), 148 (100%). HRMS (EI): Calcd. for $C_9H_8O_2$: 148.0524, found: 148.0505.



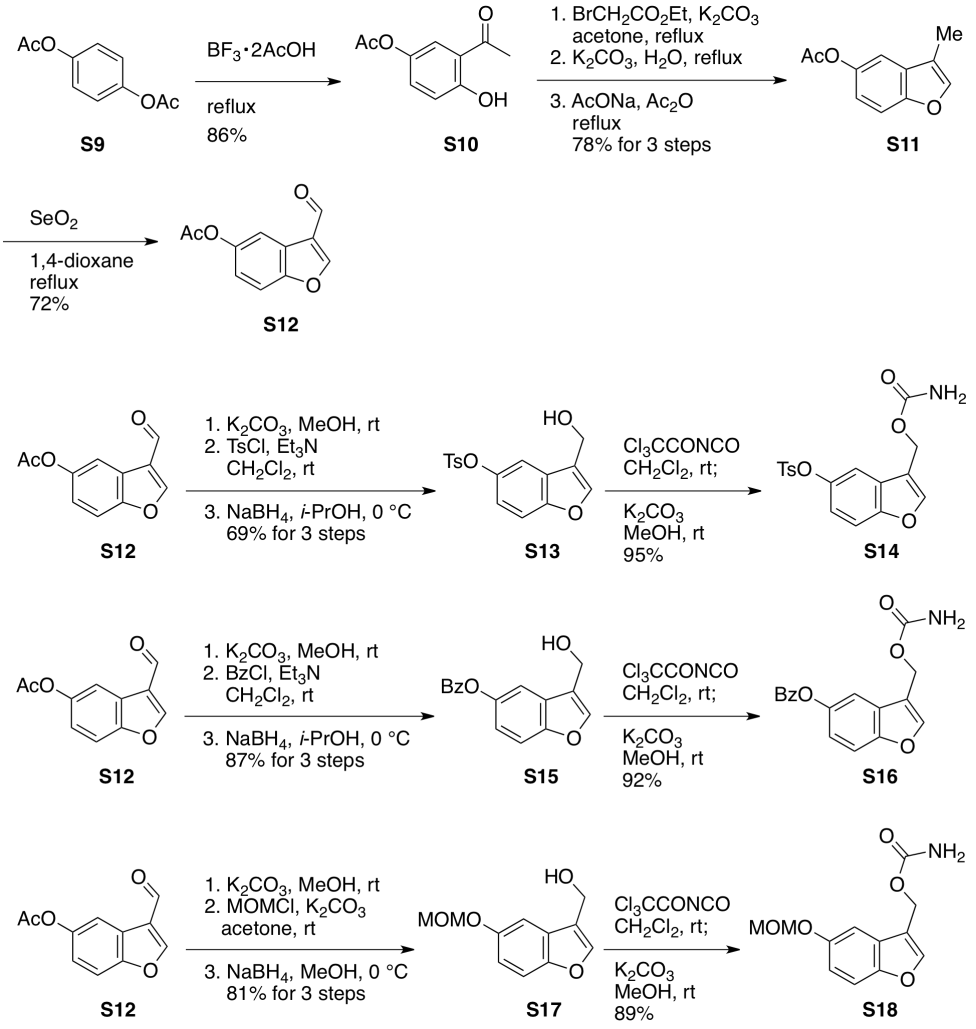
S8 **3**

Benzofuran-3-yl-methyl carbamate (**3**)[4]: To a solution of alcohol **S8** (2.11 g, 14.2 mmol) in CH_2Cl_2 (41 mL) was slowly added $Cl_3CCONCO$ (3.0 mL, 17.0 mmol) at 0 °C. The solution was stirred for 2 h at room temperature. The solvent was removed under reduced pressure, and the residue was taken up in MeOH (32 mL). To this solution was added K_2CO_3 (196 mg, 1.42 mmol), and the mixture was stirred at room temperature for 4 h. After water was added to the reaction mixture, the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by recrystallization from $CHCl_3$ to give carbamate **3** (2.19 g, 11.5 mmol, 80%) as a colorless needle.

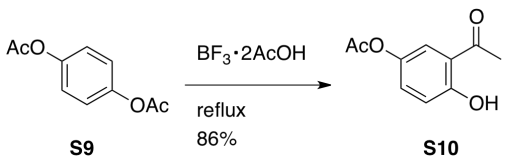
^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.02 (1H, s), 7.69 (1H, d, *J* = 7.2 Hz), 7.58 (1H, d, *J* = 8.4 Hz), 7.37-7.24 (2H, m), 6.58 (2H, br s), 5.14 (2H, s). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 156.7, 154.7,

144.6, 126.6, 124.7, 122.9, 120.3, 116.9, 111.4, 55.5. IR (neat, cm^{-1}): 3428, 3343, 3286, 3212, 3118, 1633. MS *m/z*: 191 (M^+), 148 (100%). HRMS (EI): Calcd. for $C_{10}H_9NO_3$: 191.0582, found: 191.0591.

Scheme S4: Preparation of benzofurans S14, S16, and S18.



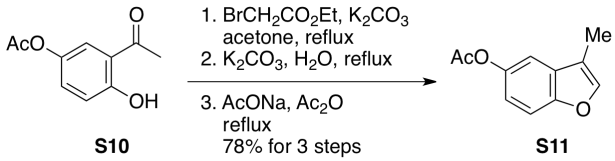
cf. BF_3•2AcOH mediated Fries rearrangement of **S9**, see: ref. (7).



5-Acetoxy-2-hydroxyacetophenone (S10)[7]: BF_3•2AcOH (103 mL, 1 M) was carefully added to neat 1,4-diacetoxybenzene (**S9**) (20.0 g, 103 mmol) at room temperature with rapid stirring. The

mixture was refluxed for 1 h. The resulting solution was allowed to cool to room temperature, and then saturated aqueous $NaHCO_3$ was added at 0 °C. The resultant mixture was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 AcOEt:Hexane) to give acetophenone **S10** (17.4 g, 89.6 mmol, 86%) as a white solid.

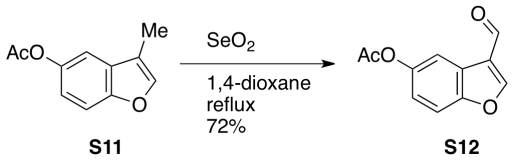
^{1}H-NMR (400 MHz, $CDCl_3$): δ 12.12 (1H, s), 7.45 (1H, d, J = 2.9 Hz), 7.21 (1H, dd, J = 9.0, 2.9 Hz), 6.99 (1H, d, J = 9.0 Hz), 2.61 (3H, s), 2.31 (3H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 203.8, 169.6, 160.0, 142.0, 130.1, 122.7, 119.3, 119.2, 26.6, 20.9. IR (neat, cm^{-1}): 3078, 2926, 1754, 1637, 1623, 1590. MS *m/z*: 194 (M^+), 152 (100%). HRMS (EI): Calcd. for $C_{10}H_{10}O_4$: 194.0579, found: 194.0580.



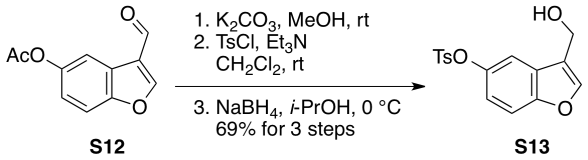
S10 **S11**

3-Methylbenzofuran-5-yl acetate (**S11**): A mixture of acetophenone **S10** (14.0 g, 72.1 mmol), ethyl bromoacetate (9.6 mL, 86.5 mmol), and K_2CO_3 (20.0 g, 144 mmol) in acetone (72 mL) was refluxed for 2 h. After cooling, the mixture was quenched with addition of aqueous HCl and the resultant solution was extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude product that was used in the next reaction without further purification. To a solution of crude product in water (120 mL) at room temperature was added K_2CO_3 (30.0 g, 216 mmol). After the reaction mixture was gently refluxed for 3 h, the solution was cooled to 0 °C, and carefully acidified with aqueous HCl. The deposited precipitate was filtered off, washed several times with cold water to provide crude carboxylic acid product that was carried on without further purification. A mixture of crude product and anhydrous AcONa (30.0 g, 361 mmol) in Ac_2O (68 mL, 721 mmol) was refluxed for 12 h. After cooling, water was added and the resultant solution was extracted with Et_2O. The combined extracts were washed with saturated aqueous Na_2CO_3, with water, and then with brine, and finally dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:30 AcOEt:Hexane) to give benzofuran **S11** (10.7 g, 56.3 mmol, 78% for 3 steps) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.43 (1H, s), 7.41 (1H, d, J = 7.8 Hz), 7.23 (1H, d, J = 2.4 Hz), 6.98 (1H, dd, J = 7.8, 2.4 Hz), 2.32 (3H, s), 2.21 (3H, d, J = 1.2 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.0, 152.8, 146.1, 142.7, 129.7, 117.8, 115.9, 112.0, 111.7, 21.0, 7.7. IR (neat, cm^{-1}): 3119, 2924, 2866, 1761, 1624, 1599. MS *m/z*: 190 (M^+), 148 (100%). HRMS (EI): Calcd. for $C_{11}H_{10}O_3$: 190.0630, found: 190.0628.



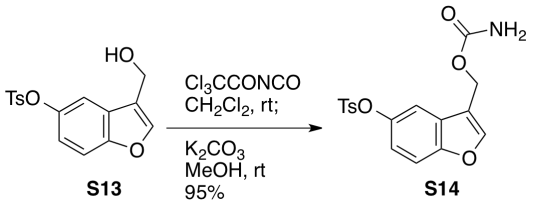
3-Formylbenzofuran-5-yl acetate (**S12**): A mixture of benzofuran **S11** (6.00 g, 31.6 mmol) and SeO_2 (17.5 g, 158 mmol) in dry 1,4-dioxane (105 mL) was refluxed for 72 h. The resulting black precipitate was filtered off, and concentrated under reduced pressure. The resulting mixture was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 to 1:1 AcOEt:Hexane) to give aldehyde **S12** (4.63 g, 22.7 mmol, 72%) as a colorless solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.15 (1H, s), 8.29 (1H, s), 7.90 (1H, d, *J* = 2.4 Hz), 7.54 (1H, d, *J* = 9.0 Hz), 7.14 (1H, dd, *J* = 9.0, 2.4 Hz), 2.33 (3H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 184.3, 169.7, 156.1, 153.4, 147.9, 123.75, 123.69, 120.4, 115.4, 112.2, 21.0. IR (neat, cm^{-1}): 3127, 3080, 2831, 2751, 1749, 1685, 1670. MS *m/z*: 204 (M^+), 162 (100%). HRMS (EI): Calcd. for $C_{11}H_8O_4$: 204.0423, found: 204.0404.



3-(Hydroxymethyl)benzofuran-5-yl 4-methylbenzenesulfonate (**S13**): To a solution of acetate **S12** (80 mg, 0.392 mmol) in MeOH (1.3 mL) was added K_2CO_3 (28 mg, 0.199 mmol) at room temperature. The resulting solution was stirred for 1 h. The solution was then added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude phenol product that was used in the next reaction without further purification. To a solution of crude phenol product in CH_2Cl_2 (2.0 mL) were added Et_3N (0.11 mL, 0.784 mmol) and TsCl (112 mg, 0.588 mmol) at 0 °C. The mixture was allowed to warm to room temperature, and stirred for 15 min. Water was added to the reaction mixture, and the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude tosylate product that was used in the next reaction without further purification. To a solution of crude tosylate product in *i*-PrOH (2.0 mL) was added $NaBH_4$ (37 mg, 0.980 mmol) at 0 °C, and the mixture was stirred for 40 min. The reaction mixture was added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:2 to 1:1 AcOEt:Hexane) to give alcohol **S13** (86 mg, 0.270 mmol, 69% for 3 steps) as a colorless

oil.

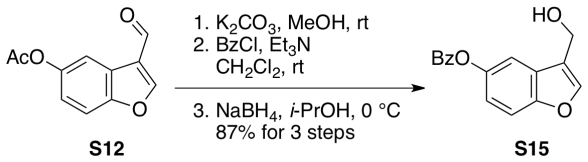
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.73-7.69 (2H, m), 7.64 (1H, s), 7.343 (1H, d, *J* = 9.0 Hz), 7.342 (1H, d, *J* = 2.4 Hz), 7.32-7.29 (2H, m), 6.87 (1H, dd, *J* = 9.0, 2.4 Hz), 4.77 (2H, dd, *J* = 5.8, 1.0 Hz), 2.45 (3H, s), 1.64 (1H, t, *J* = 5.8 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 153.6, 145.4, 145.1, 144.0, 132.2, 129.7, 128.5, 127.5, 120.8, 118.9, 113.9, 112.0, 55.4, 21.6. IR (neat, cm^{-1}): 3549, 3397, 3121, 2927, 2877, 1623, 1598. MS *m/z*: 318 (M^+), 163 (100%). HRMS (EI): Calcd. for $C_{16}H_{14}O_5S$: 318.0562, found: 318.0562.



S13 **S14**

3-(Carbamoyloxymethyl)benzofuran-5-yl 4-methylbenzenesulfonate (**S14**): To a solution of alcohol **S13** (386 mg, 1.21 mmol) in CH_2Cl_2 (3.0 mL) was slowly added $Cl_3CCONCO$ (0.26 mL, 1.46 mmol) at 0 °C. The solution was stirred for 30 min at room temperature. The solvent was removed under reduced pressure, and the residue was taken up in MeOH (3.0 mL). To this solution was added K_2CO_3 (16.7 mg, 0.121 mmol), and the mixture was stirred at room temperature for 14 h. After water was added to the reaction mixture, the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:2 to 2:1 AcOEt:Hexane) to give carbamate **S14** (416 mg, 1.15 mmol, 95%) as a colorless solid.

^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.10 (1H, s), 7.73 (2H, d, *J* = 8.0 Hz), 7.59-7.55 (1H, m), 7.46 (2H, d, *J* = 8.0 Hz), 7.40 (1H, d, *J* = 2.4 Hz), 6.89 (1H, dd, *J* = 9.2, 2.4 Hz), 6.58 (2H, br s), 5.06 (2H, s), 2.41 (3H, s). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 156.5, 152.8, 146.7, 145.8, 144.8, 131.4, 130.2, 128.2, 127.4, 118.7, 117.3, 113.8, 112.5, 55.1, 21.1. IR (neat, cm^{-1}): 3489, 3440, 3316, 3271, 3208, 3131, 1711, 1696, 1597. MS *m/z*: 361 (M^+), 163 (100%). HRMS (EI): Calcd. for $C_{17}H_{15}NO_6S$: 361.0620, found: 361.0634.

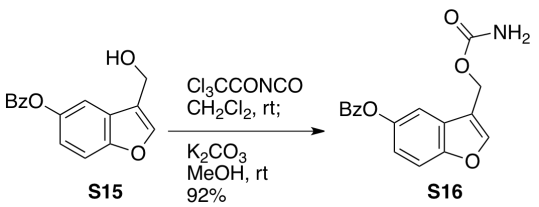


S12 **S15**

3-(Hydroxymethyl)benzofuran-5-yl benzoate (**S15**): To a solution of acetate **S12** (4.60 g, 22.5 mmol) in MeOH (56 mL) was added K_2CO_3 (623 mg, 4.51 mmol) at room temperature. The resulting solution was stirred for 4 h. The solution was then added saturated aqueous NH_4Cl, and

extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude phenol product that was used in the next reaction without further purification. To a solution of crude phenol product in CH_2Cl_2 (56 mL) were added Et_3N (7.9 mL, 56.3 mmol) and BzCl (4.0 mL, 33.8 mmol) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 1.5 h. After water was added to the reaction mixture, the resultant solution was extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude benzoate product that was used in the next reaction without further purification. To a solution of crude benzoate product in *i*-PrOH (56 mL) was added $NaBH_4$ (1.7 g, 45.1 mmol) at 0 °C, and the mixture was stirred for 2 h. The reaction mixture was added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 to 1:1 AcOEt:Hexane) to give alcohol **S15** (5.26 g, 19.6 mmol, 87% for 3 steps) as a colorless solid.

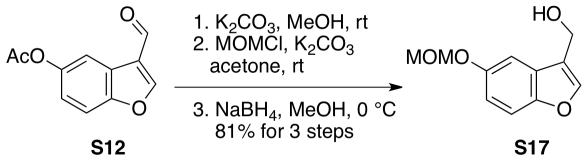
^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.22 (2H, d, *J* = 8.3 Hz), 7.67-7.61 (2H, m), 7.56-7.48 (4H, m), 7.16 (1H, dd, *J* = 8.8, 2.4 Hz), 4.82 (2H, d, *J* = 3.9 Hz), 1.73 (1H, br s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 165.7, 153.0, 146.3, 143.5, 133.5, 130.0, 129.3, 128.4, 127.4, 120.6, 118.3, 112.7, 111.9, 55.3. IR (neat, cm^{-1}): 3407, 3116, 3072, 2936, 2873, 1735, 1621, 1598. MS *m/z*: 268 (M^+), 105 (100%). HRMS (EI): Calcd. for $C_{16}H_{12}O_4$: 268.0736, found: 268.0707.



3-(Carbamoyloxymethyl)benzofuran-5-yl benzoate (**S16**): To a solution of alcohol **S15** (4.39 g, 16.4 mmol) in CH_2Cl_2 (33 mL) was slowly added $Cl_3CCONCO$ (3.5 mL, 19.6 mmol) at 0 °C. The solution was stirred for 2 h at room temperature. The solvent was removed under reduced pressure, and the residue was taken up in MeOH (33 mL). To this solution was added K_2CO_3 (227 mg, 1.64 mmol), and the mixture was stirred at room temperature for 3 h. After water was added to the reaction mixture, the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by recrystallization from 1:1 $CHCl_3$:Hexane to give carbamate **S16** (4.71 g, 15.1 mmol, 92%) as a colorless needle.

^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.18-8.14 (2H, m), 8.11 (1H, s), 7.78-7.72 (1H, m), 7.67 (1H, d, *J* = 8.8 Hz), 7.65-7.59 (2H, m), 7.59 (1H, d, *J* = 2.4 Hz), 7.26 (1H, dd, *J* = 8.8, 2.4 Hz), 6.59 (2H, br s), 5.13 (2H, s). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 165.0, 156.6, 152.4, 146.3, 146.1, 134.0, 129.7,

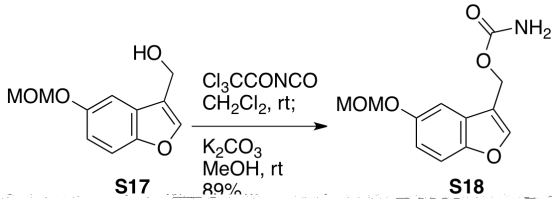
129.0, 127.4, 119.0, 117.3, 113.1, 112.1, 55.4. IR (neat, cm^{-1}): 3447, 3339, 1732, 1689, 1598. MS *m/z*: 311 (M^+), 105 (100%). HRMS (EI): Calcd. for $C_{17}H_{13}NO_5$: 311.0794, found: 311.0783.



S12 **S17**

(5-(Methoxymethoxy)benzofuran-3-yl)methanol (**S17**): To a solution of acetate **S12** (600 mg, 2.94 mmol) in MeOH (15 mL) was added K_2CO_3 (81 mg, 0.588 mmol) at room temperature. The resulting solution was stirred for 3 h. The solution was then added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude phenol product that was used in the next reaction without further purification. To a solution of crude phenol product in acetone (15 mL) were added K_2CO_3 (610 mg, 4.41 mmol) and MOMCl (0.33 mL, 4.41 mmol) at room temperature. After stirring for 20 h at room temperature, to the reaction mixture were added K_2CO_3 (610 mg, 4.41 mmol) and MOMCl (0.33 mL, 4.41 mmol) again. The mixture was stirred for another 4 h. After water was added to the reaction mixture, the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude MOM ether product that was used in the next reaction without further purification. To a solution of crude MOM ether product in MeOH (15 mL) was added $NaBH_4$ (167 mg, 45.1 mmol) at 0 °C, and the mixture was stirred for 30 min. The reaction mixture was added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:2 AcOEt:Hexane) to give alcohol **S17** (497 mg, 2.39 mmol, 81% for 3 steps) as a colorless oil.

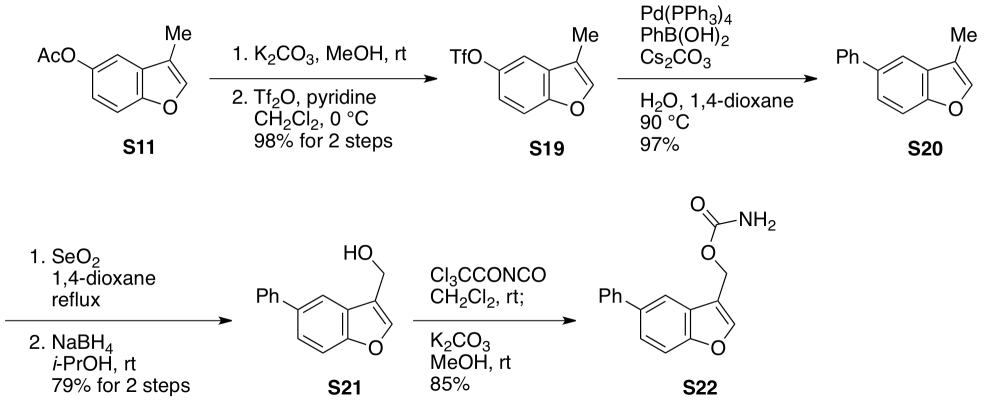
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.59 (1H, s), 7.38 (1H, d, *J* = 9.0 Hz), 7.31 (1H, d, *J* = 2.4 Hz), 7.02 (1H, dd, *J* = 9.0, 2.4 Hz), 5.20 (2H, s), 4.80 (2H, s), 3.51 (3H, s), 1.76 (1H, br s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 153.5, 151.3, 143.3, 127.3, 120.6, 115.2, 112.0, 106.3, 95.5, 55.9, 55.8. IR (neat, cm^{-1}): 3406, 3114, 2937, 2900, 2827, 1618, 1600, 1581. MS *m/z*: 208 (M^+), 208 (100%). HRMS (EI): Calcd. for $C_{11}H_{12}O_4$: 208.0736, found: 208.0739.

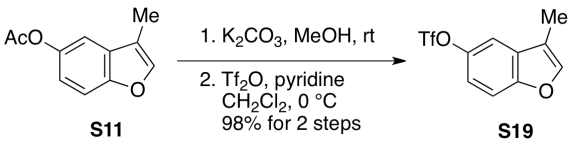


(5-(Methoxymethoxy)benzofuran-3-yl)methyl carbamate (**S18**): To a solution of alcohol **S17** (463 mg, 2.22 mmol) in CH_2Cl_2 (5.6 mL) was slowly added $Cl_3CCONCO$ (0.48 mL, 2.67 mmol) at 0 °C. The solution was stirred for 30 min at room temperature. The solvent was removed under reduced pressure, and the residue was taken up in MeOH (5.6 mL). To this solution was added K_2CO_3 (31 mg, 0.222 mmol), and the mixture was stirred at room temperature for 11 h. After water was added to the reaction mixture, the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by recrystallization from 1:1 $CHCl_3$:Hexane to give carbamate **S18** (496 mg, 1.97 mmol, 89%) as a colorless needle.

^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.98 (1H, s), 7.49 (1H, d, J = 8.9 Hz), 7.30 (1H, d, J = 2.6 Hz), 7.02 (1H, dd, J = 8.9, 2.6 Hz), 6.55 (2H, br s), 5.18 (2H, s), 5.09 (2H, s), 3.40 (3H, s). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 156.7, 153.0, 150.3, 145.6, 127.3, 117.0, 114.8, 111.9, 106.7, 94.9, 55.5. IR (neat, cm^{-1}): 3400, 3319, 3262, 3121, 2949, 2895, 1681, 1598. MS *m/z*: 251 (M^+), 146 (100%). HRMS (EI): Calcd. for $C_{12}H_{13}NO_5$: 251.0794, found: 251.0789.

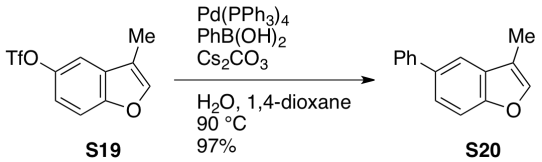
Scheme S5: Preparation of benzofuran S22.





3-Methylbenzofuran-5-yl trifluoromethanesulfonate (**S19**): To a solution of acetate **S11** (800 mg, 4.21 mmol) in MeOH (8.4 mL) was added K_2CO_3 (292 mg, 2.11 mmol) at room temperature. The resulting solution was stirred for 30 min. The solution was then added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude phenol product that was used in the next reaction without further purification. To a solution of crude phenol product in CH_2Cl_2 (14.0 mL) were added pyridine (1.3 mL, 16.8 mmol) and Tf_2O (0.87 mL, 5.47 mmol) at 0 °C, and stirred for 10 min. Saturated aqueous $NaHCO_3$ was added to the reaction mixture, and the resultant solution was extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hexane) to give trifluoromethanesulfonate **S19** (1.16 g, 4.14 mmol, 98% for 2 steps) as a colorless oil.

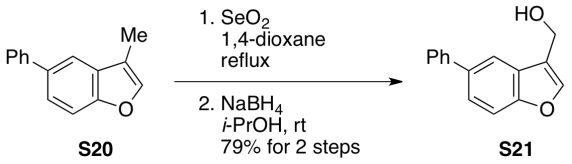
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.51 (1H, d, *J* = 1.0 Hz), 7.48 (1H, d, *J* = 8.8 Hz), 7.42 (1H, d, *J* = 2.7 Hz), 7.18 (1H, dd, *J* = 8.8, 2.7 Hz), 2.25 (3H, d, *J* = 1.0 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 153.8, 145.1, 143.9, 130.2, 118.8 (q, *J* = 320.1 Hz), 117.2, 116.2, 112.4, 112.3, 7.6. IR (neat, cm^{-1}): 3126, 2954, 2928, 2870, 1626, 1594. MS *m/z*: 280 (M^+), 147 (100%). HRMS (EI): Calcd. for $C_{10}H_7F_3O_4S$: 280.0017, found: 280.0014.



3-Methyl-5-phenylbenzofuran (**S20**)[8]: To a solution of trifluoromethanesulfonate **S19** (1.03 g, 3.68 mmol) in water (7.4 mL) and 1,4-dioxane (37.0 mL) were added $PhB(OH)_2$ (673 mg, 5.52 mmol), Cs_2CO_3 (2.40 g, 7.36 mmol) and $Pd(PPh_3)_4$ (425 mg, 0.368 mmol) at room temperature. The mixture was heated at 90 °C for 2 h. After cooling to room temperature, water was added and resultant solution was extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hexane) to give benzofuran **S20** (742 mg, 3.56 mmol, 97%) as a white solid.

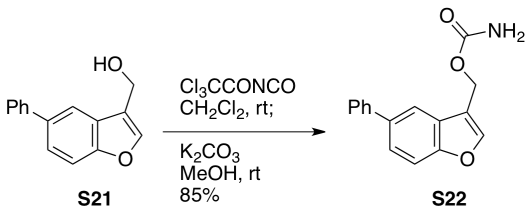
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.70 (1H, s), 7.63 (2H, d, *J* = 7.8 Hz), 7.53-7.41 (5H, m), 7.36-7.30 (1H, m), 2.27 (3H, d, *J* = 1.5 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 154.9, 142.0, 141.8, 136.0, 129.5, 128.7, 127.5, 126.8, 123.8, 118.0, 115.9, 111.4, 7.9. IR (neat, cm^{-1}): 3115, 3060, 3030, 2945, 2922, 2861, 1601. MS *m/z*: 208 (M^+), 208 (100%). HRMS (EI): Calcd. for $C_{15}H_{12}O$: 208.0888, found:

208.0879.



(5-Phenylbenzofuran-3-yl)methanol (**S21**): A mixture of benzofuran **S20** (742 mg, 3.56 mmol) and SeO_2 (2.00 g, 17.8 mmol) in 1,4-dioxane (17.8 mL) was refluxed for 46 h. The resulting black precipitate was filtered off, and concentrated under reduced pressure. The resulting mixture was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude aldehyde product that was used in the next reaction without further purification. To a solution of crude aldehyde product in *i*-PrOH (11.9 mL) was added $NaBH_4$ (269 mg, 7.12 mmol) at 0 °C. The mixture was stirred for 1 h at room temperature. The resultant solution was added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 to 1:2 AcOEt:Hexane) to give alcohol **S21** (629 mg, 2.80 mmol, 79% for 2 steps) as a white solid.

^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.95 (1H, s), 7.89 (1H, s), 7.68 (2H, d, J = 7.5 Hz), 7.64-7.56 (2H, m), 7.47 (2H, dd, J = 7.5, 7.5 Hz), 7.35 (1H, t, J = 7.5 Hz), 5.19 (1H, t, J = 5.4 Hz), 4.67 (2H, d, J = 5.4 Hz). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 154.5, 143.1, 140.7, 135.1, 128.8, 127.6, 126.9, 123.5, 121.8, 118.5, 111.5, 53.8. IR (neat, cm^{-1}): 3337, 3248, 3132, 3053, 3026, 2939, 2871. MS *m/z*: 224 (M^+), 224 (100%). HRMS (EI): Calcd. for $C_{15}H_{12}O_2$: 224.0837, found: 224.0838.

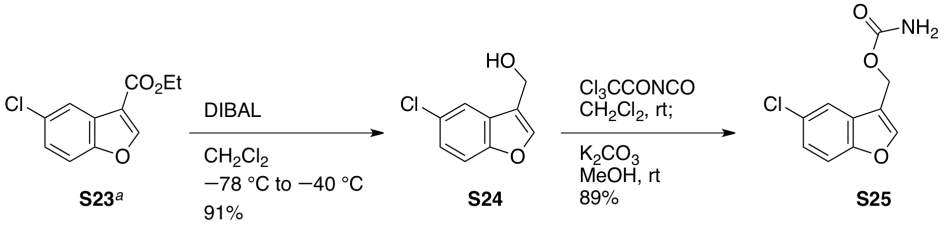


(5-Phenylbenzofuran-3-yl)methyl carbamate (**S22**): To a solution of alcohol **S21** (400 mg, 1.78 mmol) in CH_2Cl_2 (5.9 mL) was slowly added $Cl_3CCONCO$ (0.38 mL, 2.14 mmol) at 0 °C. The solution was stirred for 2 h at room temperature. The solvent was removed under reduced pressure, and the residue was taken up in MeOH (5.9 mL). To this solution was added K_2CO_3 (25.0 mg, 0.178 mmol), and the mixture was stirred at room temperature for 12 h. After water was added to the reaction mixture, the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by recrystallization from 1:1 $CHCl_3$:Hexane to give carbamate **S22** (407 mg, 1.52 mmol,

85%) as a colorless needle.

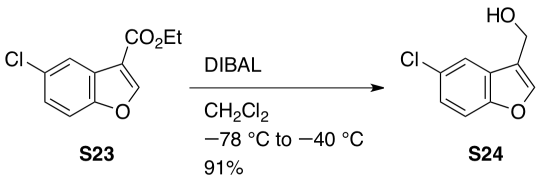
^{1}H-NMR (600 MHz, DMSO-d_6): δ 8.07 (1H, s), 7.96 (1H, s), 7.71-7.65 (3H, m), 7.62 (1H, d, J = 8.9 Hz), 7.47 (2H, dd, J = 7.6, 7.6 Hz), 7.36 (1H, t, J = 7.6 Hz), 6.66 (1H, br s), 6.57 (1H, br s), 5.20 (2H, s). ^{13}C-NMR (150 MHz, DMSO-d_6): δ 156.7, 154.4, 145.2, 140.5, 135.5, 128.9, 127.3, 127.04, 126.96, 123.8, 118.5, 117.2, 111.7, 55.5. IR (neat, cm^{-1}): 3426, 3325, 3275, 3202, 3116, 2976, 2944, 1693, 1600. MS *m/z*: 267 (M^+), 224 (100%). HRMS (EI): Calcd. for $C_{16}H_{13}NO_3$: 267.0895, found: 267.0893.

Scheme S6: Preparation of benzofuran S25.



S23[a] S24 S25

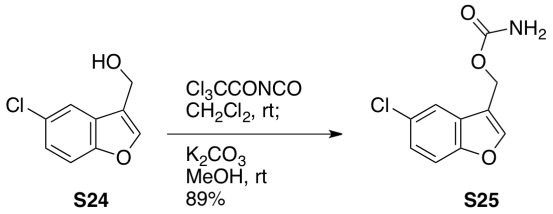
[a] Ethyl 5-chlorobenzofuran-3-carboxylate (**S23**) is commercially available.



S23 S24

(5-Chlorobenzofuran-3-yl)methanol (**S24**)[9]: To a solution of ethyl ester **S23** (490 mg, 2.18 mmol) in CH_2Cl_2 (21.8 mL) was added DIBAL (1 M in Hexane, 10.9 mL, 10.9 mmol) at −78 °C. The mixture was brought to −40 °C, and stirred 10 min. When TLC indicated consumption of the ethyl ester **S23**, water was added at −40 °C. The resulting mixture was slowly brought to room temperature. The mixture was added aqueous HCl, diluted with AcOEt, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 to 1:2 AcOEt:Hexane) to give alcohol **S24** (362 mg, 1.98 mmol, 91%) as a colorless solid.

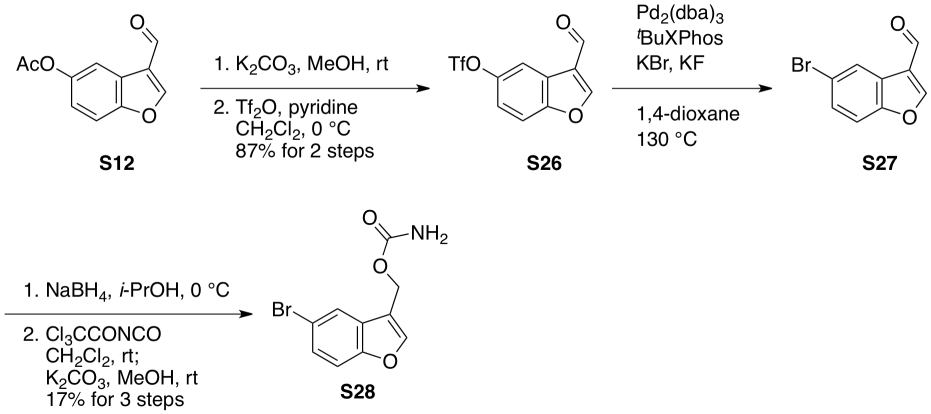
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.66 (1H, d, J = 2.0 Hz), 7.63 (1H, s), 7.41 (1H, d, J = 8.8 Hz), 7.28 (1H, dd, J = 8.8, 2.0 Hz), 4.82 (2H, d, J = 5.4 Hz), 1.60 (1H, t, J = 5.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 154.0, 143.6, 128.5, 128.1, 124.9, 120.2, 119.8, 112.6, 55.7. IR (neat, cm^{-1}): 3310, 2935, 2876, 1612, 1590. MS *m/z*: 182 (M^+), 182 (100%). HRMS (EI): Calcd. for $C_9H_7ClO_2$: 182.0135, found: 182.0118.



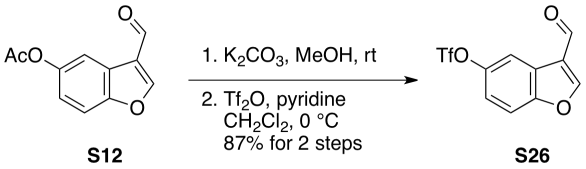
(5-Chlorobenzofuran-3-yl)methyl carbamate (**S25**): To a solution of alcohol **S24** (324 mg, 1.77 mmol) in CH_2Cl_2 (5.9 mL) was slowly added $Cl_3CCONCO$ (0.38 mL, 2.12 mmol) at 0 °C. The solution was stirred for 30 min at room temperature. The solvent was removed under reduced pressure, and the residue was taken up in MeOH (5.9 mL). To this solution was added K_2CO_3 (24.0 mg, 0.177 mmol), and the mixture was stirred at room temperature for 24 h. After water was added to the reaction mixture, the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by recrystallization from 3:1 $CHCl_3$:Hexane to give carbamate **S25** (357 mg, 1.58 mmol, 89%) as a colorless needle.

^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.11 (1H, s), 7.75 (1H, d, J = 2.0 Hz), 7.63 (1H, d, J = 8.8 Hz), 7.36 (1H, dd, J = 8.8, 2.0 Hz), 6.61 (2H, br s), 5.12 (2H, s). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 156.6, 153.3, 146.3, 128.3, 127.4, 124.6, 119.9, 116.9, 113.1, 55.2. IR (neat, cm^{-1}): 3433, 3286, 3208, 3128, 2948, 1699, 1658, 1635, 1594. MS *m/z*: 225 (M^+), 182 (100%). HRMS (EI): Calcd. for $C_{10}H_8ClNO_3$: 225.0193, found: 225.0205.

Scheme S7: Preparation of benzofuran S28.

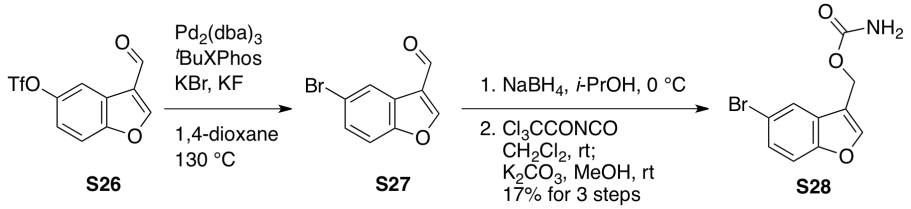


cf. Pd-catalyzed conversion of aryl triflate to bromide (**S26** → **S27**), see: ref. (10).



3-Formylbenzofuran-5-yl trifluoromethanesulfonate (**S26**): To a solution of acetate **S12** (1.50 g, 7.35 mmol) in MeOH (24.5 mL) was added K_2CO_3 (509 mg, 3.68 mmol) at room temperature. The resulting solution was stirred for 1 h. The solution was then added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude phenol product that was used in the next reaction without further purification. To a solution of crude phenol product in CH_2Cl_2 (36.8 mL) were added pyridine (2.4 mL, 29.4 mmol) and Tf_2O (1.6 mL, 9.56 mmol) at 0 °C, and stirred for 20 min. Saturated aqueous $NaHCO_3$ was added to the reaction mixture, and the resultant solution was extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:8 to 1:2 AcOEt:Hexane) to give aldehyde **S26** (1.88 g, 6.39 mmol, 87% for 2 steps) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.18 (1H, s), 8.37 (1H, s), 8.14 (1H, d, J = 2.9 Hz), 7.63 (1H, d, J = 9.2 Hz), 7.35 (1H, dd, J = 9.2, 2.9 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 183.9, 156.6, 154.3, 146.6, 124.4, 123.6, 119.8, 118.8 (q, J = 322.3 Hz), 115.7, 113.1. IR (neat, cm^{-1}): 3148, 3098, 1676. MS *m/z*: 294 (M^+), 294 (100%). HRMS (EI): Calcd. for $C_{10}H_5F_3O_5S$: 293.9810, found: 293.9798.

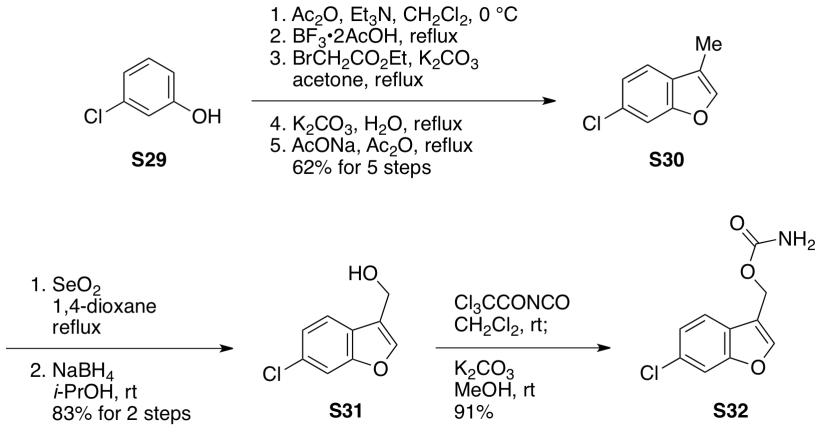


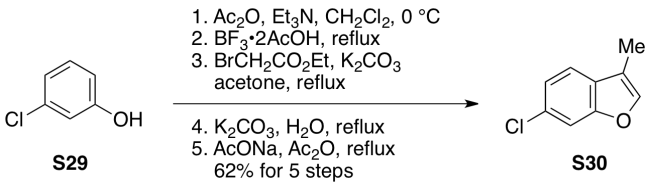
(5-Bromobenzofuran-3-yl)methyl carbamate (**S28**): To a sealed tube were added KBr (1.50 g, 12.2 mmol), KF (178 mg, 3.06 mmol), and triflate **S26** (1.80 g, 6.12 mmol). To another round-bottomed flask were added $Pd_2(dba)_3$ (560 mg, 0.612 mmol) and ^{t}BuXPhos (781 mg, 1.84 mmol), and then 1,4-dioxane (31 mL) was added *via* syringe, and the mixture was heated at 120 °C in a preheated oil bath for 3 min. After the catalyst solution was cooled to room temterature, it was added to the reaction sealed tube containing KBr and KF, and triflate **S26** *via* syringe. The resulting mixture was stirred vigorously at 130 °C in a preheated oil bath for 8 h, and then cooled to room temperature. The resultant reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:8 to 1:4 AcOEt:Hexane) to give bromide **S27** (< 681 mg, As this product include inseparable by-products, impure **S27** was used in the next

reaction without further purification). To a solution of above bromide **S27** in *i*-PrOH (31 mL) was added $NaBH_4$ (301 mg, 7.96 mmol) at 0 °C, and the mixture was stirred for 30 min. The reaction mixture was added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude alcohol product that was used in the next reaction without further purification. To a solution of crude alcohol product in CH_2Cl_2 (6.9 mL) was slowly added $Cl_3CCONCO$ (0.29 mL, 1.64 mmol) at 0 °C. The solution was stirred for 30 min at room temperature. The solvent was removed under reduced pressure, and the residue was taken up in MeOH (6.9 mL). To this solution was added K_2CO_3 (19 mg, 0.137 mmol), and the mixture was stirred at room temperature for 5 h. After water was added to the reaction mixture, the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by recrystallization from 4:1 $CHCl_3$:Hexane to give carbamate **S28** (285 mg, 1.06 mmol, 17% for 3 steps) as a colorless needle.

^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.09 (1H, s), 7.89 (1H, d, J = 2.1 Hz), 7.59 (1H, d, J = 8.7 Hz), 7.48 (1H, dd, J = 8.7, 2.1 Hz), 6.59 (2H, br s), 5.12 (2H, s). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 156.5, 153.6, 146.1, 128.9, 127.3, 122.9, 116.7, 115.3, 113.5, 55.2. IR (neat, cm^{-1}): 3404, 3320, 3261, 3184, 3125, 1681, 1595. MS *m/z*: 269 (M^+), 227 (100%). HRMS (EI): Calcd. for $C_{10}H_8BrNO_3$: 268.9688, found: 268.9682.

Scheme S8: Preparation of benzofuran S32.

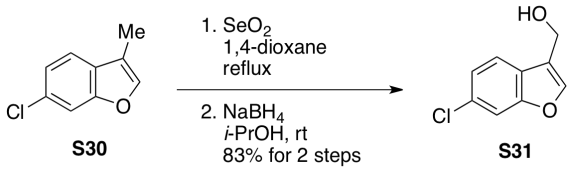




S29 **S30**

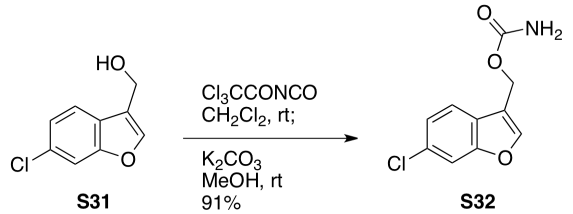
6-Chloro-3-methylbenzofuran (**S30**): To a solution of *m*-chlorophenol **S29** (4.00 g, 31.1 mmol) in CH_2Cl_2 (31.0 mL) were added Ac_2O (4.4 mL, 46.7 mmol) and Et_3N (17.2 mL, 124 mmol) at 0 °C, and stirred for 40 min. The resultant solution was then added water, and extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude acetate product that was used in the next reaction without further purification. To a crude acetate product was carefully added BF_3•2AcOH (31.0 mL, 1 M) at room temperature. The mixture was refluxed for 1 h. The resulting solution was allowed to cool to room temperature, and then saturated aqueous $NaHCO_3$ was added at 0 °C. The resultant mixture was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude α-hydroxy-acetophenone product that was used in the next reaction without further purification. To a solution of crude α-hydroxy-acetophenone product in acetone (39.0 mL) were added K_2CO_3 (17.1 g, 124 mmol), $BrCH_2CO_2Et$ (3.8 mL, 34.2 mmol) at room temperature. The resulting mixture was refluxed for 1.5 h. After cooling, the mixture was quenched with addition of saturated aqueous NH_4Cl, and the resultant solution was extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude product that was used in the next reaction without further purification. To a solution of crude product in water (62 mL) was added K_2CO_3 (30.0 g, 216 mmol) at room temperature. After the reaction mixture was gently refluxed for 10 h, the solution was cooled to 0 °C, and carefully acidified with aqueous HCl. The deposited precipitate was filtered off, washed several times with cold water to provide crude carboxylic acid product that was carried on without further purification. A mixture of crude product and anhydrous AcONa (12.8 g, 156 mmol) in Ac_2O (29.4 mL, 311 mmol) was refluxed for 14 h. After cooling, saturated aqueous $NaHCO_3$ was added and the resultant solution was extracted with hexane. The combined extracts were washed with saturated aqueous $NaHCO_3$, with water, and then with brine, and finally dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hexane) to give benzofuran **S30** (3.22 g, 19.3 mmol, 62% for 5 steps) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.46 (1H, d, J = 2.0 Hz), 7.41 (1H, d, J = 8.3 Hz), 7.39 (1H, s), 7.22 (1H, dd, J = 8.3, 2.0 Hz), 2.22 (3H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 155.3, 142.0, 130.0, 127.7, 122.9, 119.9, 115.5, 111.8, 7.7. IR (neat, cm^{-1}): 3121, 3066, 2967, 2947, 2925, 2890, 2865, 1620. MS *m/z*: 166 (M^+), 166 (100%). HRMS (EI): Calcd. for C_9H_7ClO: 166.0185, found: 166.0192.



(6-Chlorobenzofuran-3-yl)methanol (**S31**): A mixture of benzofuran **S30** (1.00 g, 6.00 mmol) and SeO_2 (3.30 g, 30.0 mmol) in 1,4-dioxane (15.0 mL) was refluxed for 50 h. The resulting black precipitate was filtered off, and concentrated under reduced pressure. The resulting mixture was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude aldehyde product that was used in the next reaction without further purification. To a solution of crude aldehyde product in *i*-PrOH (11.9 mL) was added $NaBH_4$ (454 mg, 12.0 mmol) at 0 °C. The mixture was stirred for 30 min at room temperature. The resultant solution was added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:2 to 1:1 AcOEt:Hexane) to give alcohol **S31** (908 mg, 4.97 mmol, 83% for 2 steps) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.59 (1H, s), 7.57 (1H, d, *J* = 8.3 Hz), 7.50 (1H, d, *J* = 1.5 Hz), 7.25 (1H, dd, *J* = 8.3, 1.5 Hz), 4.81 (2H, dd, *J* = 5.4, 1.0 Hz), 1.71 (1H, t, *J* = 5.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 155.7, 142.9, 130.6, 125.4, 123.6, 120.6, 120.4, 112.2, 55.8. IR (neat, cm^{-1}): 3258, 2935, 2857, 1614, 1594, 1573. MS *m/z*: 182 (M^+), 182 (100%). HRMS (EI): Calcd. for $C_9H_7ClO_2$: 182.0135, found: 182.0118.

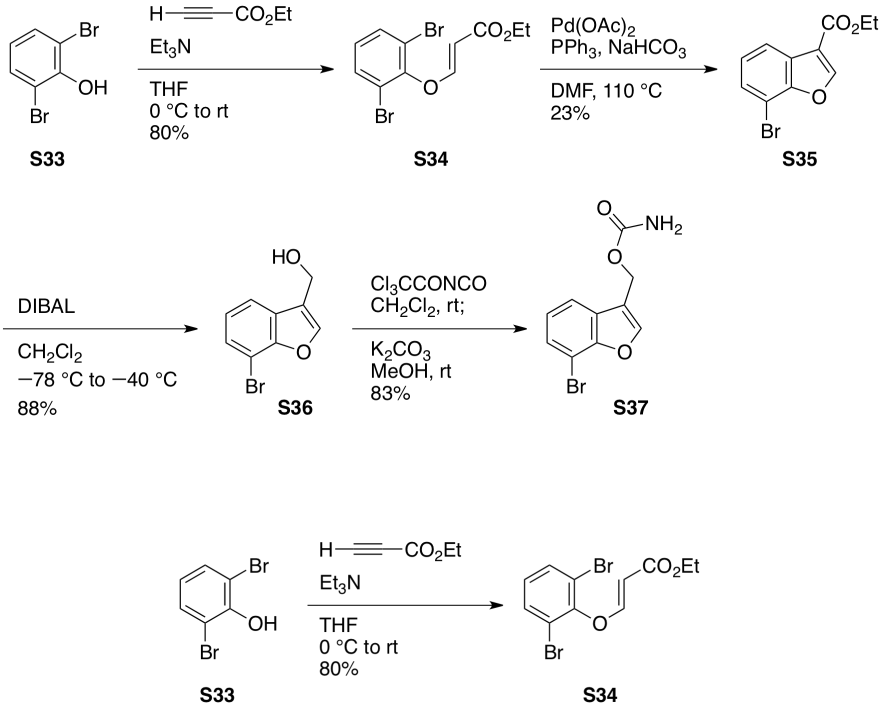


(6-Chlorobenzofuran-3-yl)methyl carbamate (**S32**): To a solution of alcohol **S31** (500 mg, 2.74 mmol) in CH_2Cl_2 (9.1 mL) was slowly added $Cl_3CCONCO$ (0.59 mL, 3.29 mmol) at 0 °C. The solution was stirred for 30 min at room temperature. The solvent was removed under reduced pressure, and the residue was taken up in MeOH (9.1 mL). To this solution was added K_2CO_3 (38.0 mg, 0.274 mmol), and the mixture was stirred at room temperature for 14 h. After water was added to the reaction mixture, the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by recrystallization from 4:1 $CHCl_3$:Hexane to give carbamate **S32** (564 mg, 2.50 mmol, 91%) as a colorless needle.

^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.07 (1H, s), 7.77 (1H, d, *J* = 1.5 Hz), 7.69 (1H, d, *J* = 8.3 Hz),

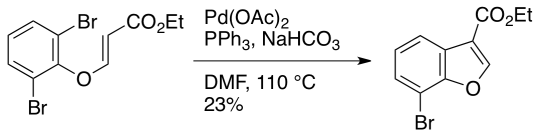
7.34 (1H, dd, J = 8.3, 1.5 Hz), 6.60 (2H, br s), 5.12 (2H, s). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 156.6, 154.9, 145.6, 129.4, 125.7, 123.4, 121.4, 117.0, 111.9, 55.3. IR (neat, cm^{-1}): 3430, 3338, 3288, 3207, 3120, 1699, 1634. MS *m/z*: 225 (M^+), 182 (100%). HRMS (EI): Calcd. for $C_{10}H_8ClNO_3$: 225.0193, found: 225.0207.

Scheme S9: Preparation of benzofuran S37.



(*E*)-Ethyl 3-(2,6-dibromophenoxy)acrylate (**S34**): To a solution of ethyl propiolate (1.2 mL, 11.9 mmol) in THF (16 mL) were added solutions of Et_3N (1.7 mL, 11.9 mmol) in THF (7.0 mL) and 2,6-dibromophenol (**S33**) (3.0 g, 11.9 mmol) in THF (7.0 mL) at 0 °C. After stirring for 1 h at 0 °C, the mixture was allowed to warm up to room temperature and stirred for another 4 h. After the reaction mixture was diluted with Et_2O and water, the resultant solution was extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:20 AcOEt:Hexane) to give ethyl ester **S34** (3.32 g, 9.49 mmol, 80%) as a colorless oil.

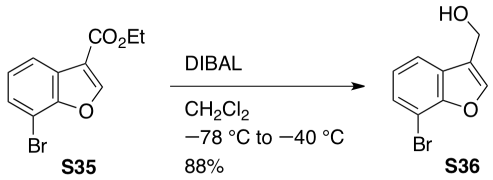
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.62 (1H, d, J = 12.4 Hz), 7.58 (2H, d, J = 8.0 Hz), 7.02 (1H, t, J = 8.0 Hz), 5.18 (1H, d, J = 12.4 Hz), 4.18 (2H, q, J = 7.2 Hz), 1.28 (3H, t, J = 7.2 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 166.6, 158.7, 149.0, 133.0, 128.2, 117.2, 101.3, 60.2, 14.2. IR (neat, cm^{-1}): 3081, 2980, 2936, 2909, 1713, 1649, 1634. MS *m/z*: 348 (M^+), 269 (100%). HRMS (EI): Calcd. for $C_{11}H_{10}Br_2O_3$: 347.8997, found: 347.8996.



S34 **S35**

Ethyl 7-bromobenzofuran-3-carboxylate (**S35**): To a solution of ethyl ester **S34** (1.50 g, 4.29 mmol) in DMF (43 mL) were added PPh_3 (900 mg, 3.43 mmol), $NaHCO_3$ (360 mg, 4.29 mmol) and $Pd(OAc)_2$ (386 mg, 1.72 mmol) at room temperature. The mixture was heated at 110 °C in a preheated oil bath for 3 h. After cooling to room temperature, the mixture was filtered through a Celite pad, and the Celite layer was washed several times with AcOEt. The filtrate was concentrated under reduced pressure. The residue was diluted with Et_2O and water, and the resultant solution was extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:20 to 1:8 AcOEt:Hexane) and recycling GPC to give benzofuran **S35** (270 mg, 1.00 mmol, 23%) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.30 (1H, s), 8.02 (1H, d, J = 7.6 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.24 (1H, dd, J = 7.6, 7.6 Hz), 4.42 (2H, q, J = 7.0 Hz), 1.43 (3H, t, J = 7.0 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 162.9, 152.7, 151.2, 128.4, 126.1, 125.5, 121.3, 115.6, 104.3, 60.8, 14.3. IR (neat, cm^{-1}): 3152, 3104, 2982, 2936, 2899, 1722, 1611. MS *m/z*: 268 (M^+), 223 (100%). HRMS (EI): Calcd. for $C_{11}H_9BrO_3$: 267.9735, found: 267.9734.

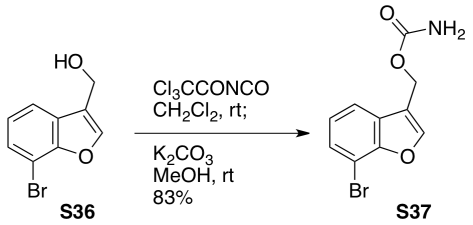


S35 **S36**

(7-Bromobenzofuran-3-yl)methanol (**S36**): To a solution of ethyl ester **S35** (225 mg, 0.948 mmol) in CH_2Cl_2 (9.5 mL) was added DIBAL (1.02 M in toluene, 4.6 mL, 4.74 mmol) at −78 °C. The mixture was brought to −40 °C, and stirred 10 min. When TLC indicated consumption of the ethyl ester **S35**, water was added at −40 °C. The resulting mixture was slowly brought to room temperature. The mixture was added aqueous HCl, diluted with AcOEt, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 to 1:2 AcOEt:Hexane) to give alcohol **S36** (189 mg, 0.832 mmol, 88%) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.69 (1H, s), 7.62 (1H, d, J = 7.7 Hz), 7.49 (1H, d, J = 7.7 Hz), 7.16 (1H, dd, J = 7.7, 7.7 Hz), 4.84 (2H, d, J = 5.8 Hz), 1.60 (1H, t, J = 5.8 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 152.8, 142.9, 128.0, 127.8, 124.2, 121.3, 119.2, 104.4, 55.9. IR (neat, cm^{-1}): 3312, 3224, 3118, 2922, 2865, 1646, 1611, 1587. MS *m/z*: 226 (M^+), 226 (100%). HRMS (EI): Calcd. for

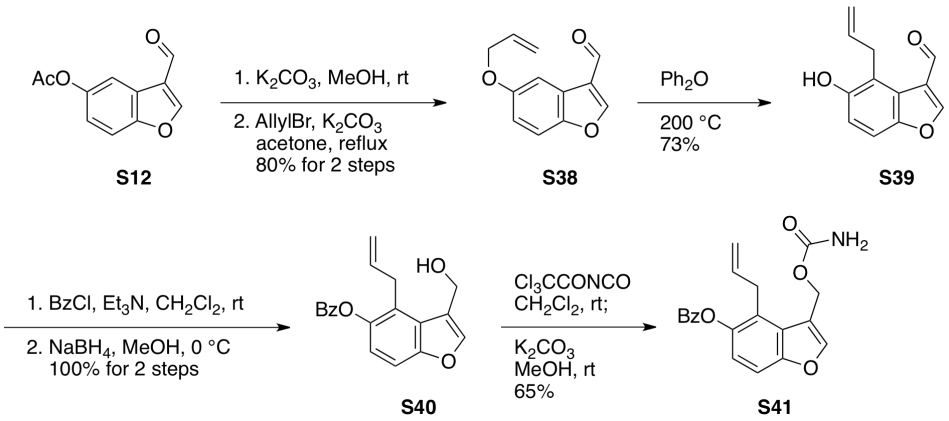
$C_9H_7BrO_2$: 225.9629, found: 225.9628.

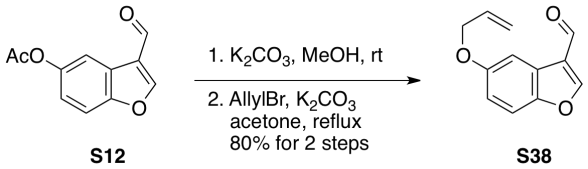


(7-Bromobenzofuran-3-yl)methyl carbamate (**S37**): To a solution of alcohol **S36** (303 mg, 1.33 mmol) in CH_2Cl_2 (4.4 mL) was slowly added $Cl_3CCONCO$ (0.28 mL, 1.60 mmol) at 0 °C. The solution was stirred for 30 min at room temperature. The solvent was removed under reduced pressure, and the residue was taken up in MeOH (4.4 mL). To this solution was added K_2CO_3 (18 mg, 0.133 mmol), and the mixture was stirred at room temperature for 5 h. After water was added to the reaction mixture, the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by recrystallization from 1:1 $CHCl_3$:Hexane to give carbamate **S37** (300 mg, 1.11 mmol, 83%) as a colorless needle.

^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.14 (1H, s), 7.71 (1H, dd, J = 7.7, 1.0 Hz), 7.58 (1H, dd, J = 7.7, 1.0 Hz), 7.24 (1H, dd, J = 7.7, 7.7 Hz), 6.58 (2H, br s), 5.13 (2H, s). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 156.5, 151.6, 145.4, 128.1, 127.5, 124.6, 119.9, 117.9, 103.3, 55.4. IR (neat, cm^{-1}): 3398, 3321, 3267, 3185, 3126, 1683, 1599. MS *m/z*: 269 (M^+), 226 (100%). HRMS (EI): Calcd. for $C_{10}H_8BrNO_3$: 268.9688, found: 268.9691.

Scheme S10: Preparation of benzofurans S41.

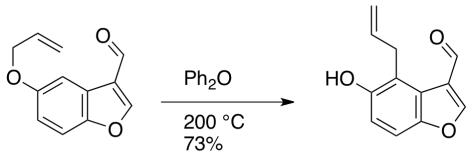




S12 **S38**

5-(Allyloxy)benzofuran-3-carbaldehyde (**S38**): To a solution of acetate **S12** (1.72 g, 8.42 mmol) in MeOH (42 mL) was added K_2CO_3 (233 mg, 1.68 mmol) at room temperature. The resulting solution was stirred for 4 h. The solution was added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude phenol product that was used in the next reaction without further purification. A mixture of crude phenol product, anhydrous K_2CO_3 (3.0 g, 21.9 mmol), and AllylBr (0.93 mL, 11.0 mmol) in acetone (42 mL) was refluxed for 4 h. After cooling, water was added and the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:8 AcOEt:Hexane) to give aldehyde **S38** (1.36 g, 6.73 mmol, 80% for 2 steps) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.14 (1H, s), 8.23 (1H, s), 7.65 (1H, d, *J* = 2.7 Hz), 7.44 (1H, d, *J* = 9.2 Hz), 7.03 (1H, dd, *J* = 9.2, 2.7 Hz), 6.09 (1H, ddt, *J* = 17.4, 10.6, 5.3 Hz), 5.45 (1H, ddt, *J* = 17.4, 1.4, 1.4 Hz), 5.31 (1H, ddt, *J* = 10.6, 1.4, 1.4 Hz), 4.61 (2H, ddd, *J* = 5.3, 1.4, 1.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 184.8, 156.5, 155.9, 151.0, 133.1, 123.9, 123.6, 117.8, 116.3, 112.3, 105.4, 69.6 IR (neat, cm^{-1}): 3130, 3082, 3021, 2984, 2912, 2825, 2742, 1681, 1615, 1599. MS *m/z*: 202 (M^+), 202 (100%). HRMS (EI): Calcd. for $C_{12}H_{10}O_3$: 202.0630, found: 202.0624.

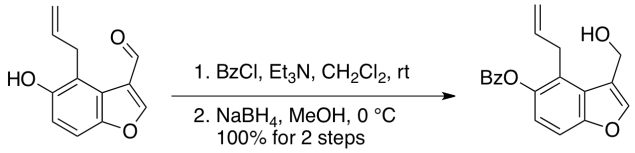


S38 **S39**

4-Allyl-5-hydroxybenzofuran-3-carbaldehyde (**S39**): A round-bottomed flask was charged with aldehyde **S38** (4.28 g, 21.2 mmol) and Ph_2O (42 mL). The mixture was heated at 200 °C for 6 h. After cooling, water was added and the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 to 1:2 AcOEt:Hexane) to give phenol **S39** (3.12 g, 15.4 mmol, 73%) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.02 (1H, s), 8.26 (1H, s), 7.34 (1H, d, *J* = 8.8 Hz), 6.97 (1H, d, *J* = 8.8 Hz), 6.08 (1H, ddt, *J* = 17.1, 10.2, 5.9 Hz), 5.17-5.11 (2H, m), 5.07 (1H, dd, *J* = 17.1, 1.5 Hz), 4.13 (2H, ddd, *J* = 5.9, 1.5, 1.5 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 184.3, 158.7, 151.8, 151.7, 136.3, 125.2, 123.2, 119.0, 115.6, 115.5, 110.5, 32.5. IR (neat, cm^{-1}): 3315, 3116, 3079, 3054, 3005,

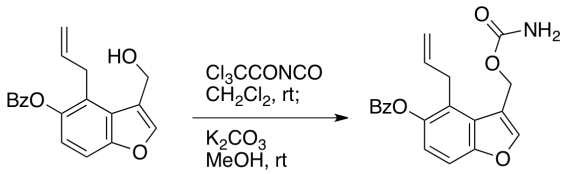
2977, 2917, 2855, 2829, 2754, 2683, 1669, 1637, 1590. MS *m/z*: 202 (M^+), 173 (100%). HRMS (EI): Calcd. for $C_{12}H_{10}O_3$: 202.0630, found: 202.0629.



S39 **S40**

4-Allyl-3-(hydroxmethyl)benzofuran-5yl benzoate (**S40**): To a solution of phenol **S39** (800 mg, 3.96 mmol) in CH_2Cl_2 (20.0 mL) were added Et_3N (1.4 mL, 9.90 mmol) and BzCl (690 μL, 5.94 mmol) at 0 °C. The mixture was allowed to warm to room temperature, and stirred for 2.5 h. The resulting solution was added water, and extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to provide crude benzoate product that was used in the next reaction without further purification. To a solution of crude benzoate product in MeOH (20.0 mL) was added $NaBH_4$ (225 mg, 5.94 mmol) at 0 °C, and stirred for 30 min. The resultant mixture was added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 to 1:2 AcOEt:Hexane) to give alcohol **S40** (1.22 g, 3.96 mmol, 100% for 2 steps) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.25-8.20 (2H, m), 7.68-7.62 (1H, m), 7.65 (1H, s), 7.56-7.50 (2H, m), 7.43 (1H, d, *J* = 8.7 Hz), 7.15 (1H, d, *J* = 8.7 Hz), 6.07-5.96 (1H, m), 5.03-4.98 (1H, m), 4.90-4.83 (1H, m), 4.82 (2H, s), 3.75-3.71 (2H, m), 1.71 (1H, br s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 165.6, 153.9, 145.0, 144.5, 136.2, 133.6, 130.2, 129.5, 128.6, 126.5, 124.7, 121.2, 119.6, 115.7, 110.4, 56.3, 31.1. IR (neat, cm^{-1}): 3454, 3077, 3008, 2978, 2925, 2878, 1735, 1637, 1601, 1582. MS *m/z*: 308 (M^+), 105 (100%). HRMS (EI): Calcd. for $C_{19}H_{16}O_4$: 308.1049, found: 308.1042.



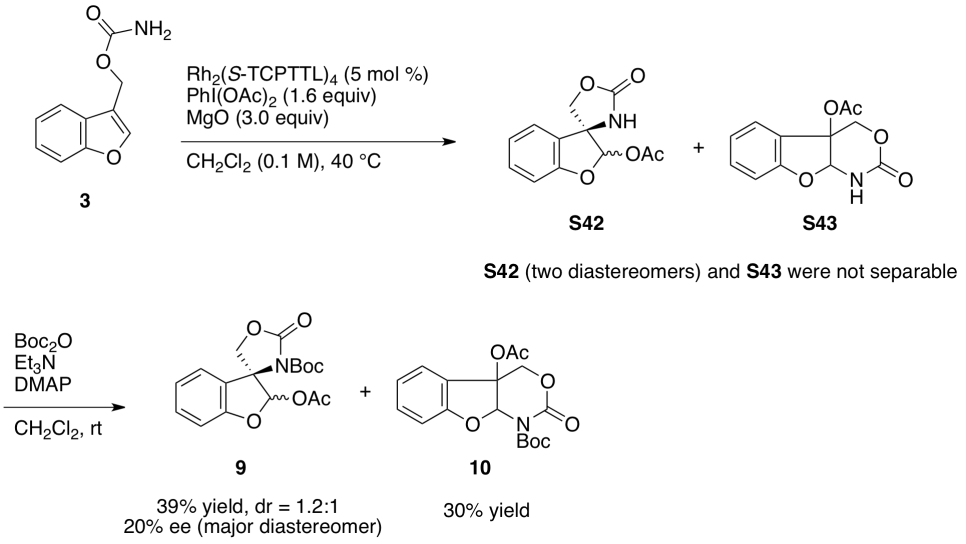
S40 **S41**

4-Allyl-3-(carbamoyloxymethyl)benzofuran-5-yl benzoate (**S41**): To a solution of alcohol **S40** (1.00 g, 3.24 mmol) in CH_2Cl_2 (16.2 mL) was slowly added $Cl_3CCONCO$ (0.69 mL, 3.89 mmol) at 0 °C. The solution was stirred for 3 h at room temperature. The solvent was removed under reduced pressure, and the residue was taken up in MeOH (16.2 mL). To this solution was added K_2CO_3 (45.0 mg, 0.0.324 mmol), and the mixture was stirred at room temperature for 20 h. After water was added

to the reaction mixture, the resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by recrystallization from 1:1 $CHCl_3$:Hexane to give carbamate **S41** (733 mg, 2.09 mmol, 65%) as a colorless needle.

^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.15 (2H, d, J = 7.6 Hz), 8.12 (1H, s), 7.76 (1H, t, J = 7.6 Hz), 7.62 (2H, dd, J = 7.6, 7.6 Hz), 7.58 (1H, d, J = 8.8 Hz), 7.25 (1H, d, J = 8.8 Hz), 6.61 (2H, br s), 5.94 (1H, ddt, J = 17.1, 10.2, 5.4 Hz), 5.08 (2H, s), 4.94 (1H, dd, J = 10.2, 1.5 Hz), 4.79 (1H, dd, J = 17.1, 1.5 Hz), 3.57 (2H, br d, J = 5.4 Hz). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 164.9, 156.3, 153.0, 146.9, 144.8, 136.0, 134.0, 129.7, 129.0, 128.9, 126.1, 124.3, 119.9, 116.8, 115.6, 110.4, 56.4, 30.6. IR (neat, cm^{-1}): 3430, 3325, 3275, 3107, 3016, 2962, 1736, 1695. MS *m/z*: 351 (M^+), 105 (100%). HRMS (EI): Calcd. for $C_{20}H_{17}NO_5$: 351.1107, found: 351.1097.

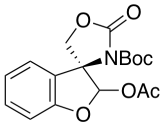
Aza-spirroannulation reaction of benzofuran 3 with Rh_2(*S*-TCPTTL)$_4$ and PhI(OAc)$_2$ (Scheme 2)



To a solution of carbamate **3** (40.0 mg, 0.209 mmol) in CH_2Cl_2 (2.1 mL) were added MgO (25.0 mg, 0.627 mmol), PhI(OAc)$_2$ (108 mg, 0.335 mmol) and Rh_2(*S*-TCPTTL)$_4$•2AcOEt (19.0 mg, 0.00105 mmol) at room temperature. The reaction mixture was stirred vigorously at 40 °C for 12 h. After cooling to room temperature, the mixture was filtered through a Celite pad. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:1 to 2:1 AcOEt:Hexane) to give a mixture of **S42** (two diastereomers) and **S43**. This mixture was used in the next reaction without further purification, as these products (**S42** and **S43**) were not separable. To a solution of a mixture of **S42** and **S43** in CH_2Cl_2 (2 mL) were added Et_3N (15 drops, excess), Boc_2O (15 drops, excess) and DMAP (5.0 mg, 0.0409 mmol) at 0 °C. The mixture was

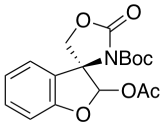
allowed to warm to room temperature, and stirred for 30 min. When TLC indicated consumption of **S42** and **S43**, water was added. The resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:3 to 1:1 AcOEt:Hexane) to give cyclic carbamates **9** (15.6 mg, 0.0447 mmol, 21% for 2 steps) as a white solid, **9'** (13.3 mg, 0.0381 mmol, 18% for 2 steps) as a white solid, and **10** (21.9 mg, 0.0627 mmol, 30% for 2 steps) as a colorless oil.

***tert*-Butyl 2-acetoxy-2'-oxo-2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxyrate (major diastereomer) (9)**



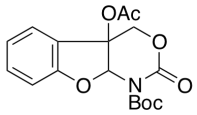
^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.35-7.31 (1H, m), 7.21 (1H, dd, *J* = 7.3, 0.9 Hz), 7.03-6.99 (1H, m), 6.95 (1H, d, *J* = 8.2 Hz), 6.73 (1H, s), 4.99 (1H, d, *J* = 10.1 Hz), 4.37 (1H, d, *J* = 10.1 Hz), 2.49 (3H, s), 1.54 (9H, s). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 169.9, 159.2, 153.0, 151.1, 131.7, 123.8, 122.5, 122.4, 110.7, 102.4, 84.6, 71.0, 68.1, 27.6, 24.6. IR (neat, cm^{-1}): 1795, 1757, 1707. MS *m/z*: 349 (M^+), 57 (100%). HRMS (EI): Calcd. for $C_{17}H_{19}NO_7$ (M^+): 349.1162, found: 349.1174. The enantiomeric excess of **9** was determined to be 20% by chiral HPLC analysis using a CHIRALPAK AD-H (1:10 *i*-PrOH:Hexane, 0.5 mL/min): 22.8 min (major enantiomer), 33.3 min (minor enantiomer).

***tert*-Butyl 2-acetoxy-2'-oxo-2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxyrate (minor diastereomer) (9')**



^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.39-7.34 (1H, m), 7.31-7.29 (1H, m), 7.10-7.05 (1H, m), 6.91 (1H, d, *J* = 7.8 Hz), 6.86 (1H, s), 4.94 (1H, d, *J* = 9.9 Hz), 4.30 (1H, d, *J* = 9.9 Hz), 2.22 (3H, s), 1.24 (9H, s). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 168.6, 158.9, 151.6, 147.7, 131.8, 124.3, 123.2, 122.7, 110.8, 100.9, 85.3, 71.1, 67.5, 27.4, 20.8. IR (neat, cm^{-1}): 3025, 2982, 2935, 1825, 1766, 1733, 1605. MS *m/z*: 349 (M^+), 206 (100%). HRMS (EI): Calcd. for $C_{17}H_{19}NO_7$ (M^+): 349.1162, found: 349.1158. The enantiomeric excess of **9'** was not determined.

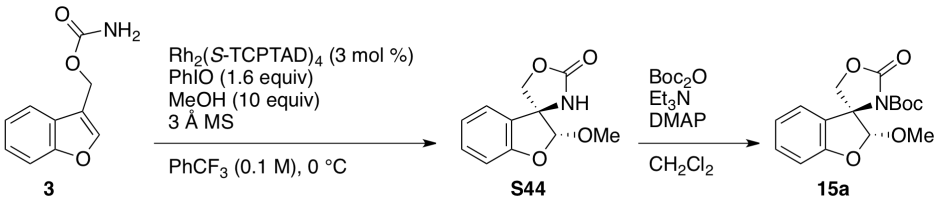
***tert*-Butyl 4a-acetoxy-2-oxo-2,4,4a,9a-tetrahydro-1*H*-benzofuro[2,3-*d*][1,3]oxazine-1-carboxylate (10)**



^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.35 (1H, dd, *J* = 7.8, 1.5 Hz), 7.36-7.31 (1H, m), 7.02 (1H, ddd, *J* = 7.8, 7.8, 1.0 Hz), 6.90 (1H, d, *J* = 7.8 Hz), 6.58 (1H, s), 4.93 (1H, d, *J* = 11.0 Hz), 4.56 (1H, d, *J* = 11.0 Hz), 2.10 (3H, s), 1.59 (9H, s). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 169.5, 160.5, 151.3, 149.3, 132.5, 126.1, 122.34, 122.30, 110.8, 91.7, 85.3, 84.8, 68.1, 27.9, 21.2. IR (neat, cm^{-1}): 3027, 2983, 2941, 1808, 1784, 1742, 1605. MS *m/z*: 349 (M^+), 145 (100%). HRMS (EI): Calcd. for $C_{17}H_{19}NO_7$ (M^+): 349.1162, found: 349.1159.

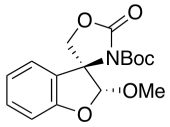
Aza-spiroannulation reaction onto benzofurans

The procedure for aza-spiroannulation of the benzofuran 3 (Table 1 entry 7: 700 mg scale)



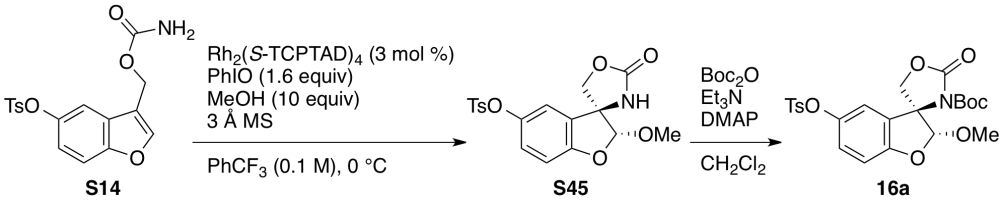
In a round-bottomed flask was charged with carbamate **3** (700 mg, 3.66 mmol) and $PhCF_3$ (36.6 mL). To this solution were added PhIO (1.29 g, 5.86 mmol), 3 Å MS (2.80 g), MeOH (1.48 mL, 36.6 mmol) at room temperature. After cooling to 0 °C, Rh_2(*S*-TCPTAD)$_4$ (232 mg, 0.110 mmol) was added. The reaction mixture was stirred vigorously at 0°C for 16 h. The resulting solution was filtered through a Celite pad. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:1 to 2:1 AcOEt:Hexane) to give carbamate **S44**. To a solution of **S44** in CH_2Cl_2 (18.3 mL) were added Et_3N (0.80 mL, 5.49 mmol), Boc_2O (1.3 mL, 5.49 mmol) and DMAP (45.0 mg, 0.366 mmol) at 0 ℃. The mixture was allowed to warm to room temperature and stirred for 30 min. When TLC indicated consumption of **S44**, water was added. The resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 to 1:2 AcOEt:Hexane) to give cyclic carbamate **15a** (812 mg, 2.53 mmol, 69% for 2 steps, 86% ee) as a white solid.

***tert*-Butyl 2-methoxy-2'-oxo-2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (15a)**



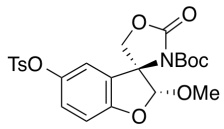
$[\alpha]_D^{29}$ –175.1° (*c* 0.51, $CHCl_3$) for 86% ee. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.32 (1H, dd, *J* = 7.6, 7.6 Hz), 7.24 (1H, d, *J* = 7.6 Hz), 7.00 (1H, dd, *J* = 7.6, 7.6 Hz), 6.84 (1H, d, *J* = 7.6 Hz), 5.67 (1H, s), 5.08 (1H, d, *J* = 9.3 Hz), 4.15 (1H, d, *J* = 9.3 Hz), 3.68 (3H, s), 1.22 (9H, s). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 159.3, 152.2, 148.1, 131.5, 125.0, 123.3, 121.8, 110.6, 109.9, 84.8, 71.2, 67.3, 57.6, 27.5. IR (neat, cm^{-1}): 2981, 2941, 1803, 1719, 1604. MS *m/z*: 321 (M^+), 177 (100%). HRMS (EI): Calcd. for $C_{16}H_{19}NO_6$ (M^+): 321.1212, found: 321.1217. The enantiomeric excess of **15a** was determined to be 86% by chiral HPLC analysis using a CHIRALPAK AD-H (1:3 *i*-PrOH:Hexane, 0.5 mL/min): 12.5 min (major enantiomer), 19.2 min (minor enantiomer).

Typical procedures for aza-spiroannulation onto benzofurans (Table 1 entries 1–6, Figure 3, Table S1-S3, Scheme S1, Scheme S2, Scheme S11)



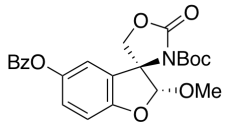
In a round-bottomed flask was charged with carbamate **S14** (50 mg, 0.138 mmol) and $PhCF_3$ (1.4 mL). To this solution were added PhIO (49.0 g, 0.221 mmol), 3 Å MS (200 mg), MeOH (56 μL, 1.38 mmol) at room temperature. After cooling to 0 °C, Rh_2(*S*-TCPTAD)$_4$ (8.7 mg, 0.00414 mmol) was added. The reaction mixture was stirred vigorously at 0°C for 48 h. The resulting solution was filtered through a Celite pad. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:1 AcOEt:Hexane) to give carbamate **S50**. To a solution of **S45** in CH_2Cl_2 (2.0 mL) were added Et_3N (15 drops, excess), Boc_2O (15 drops, excess) and DMAP (3.0 mg, 0.0246 mmol) at 0 ℃. The mixture was allowed to warm to room temperature, and stirred for 30 min. When TLC indicated consumption of **S45**, water was added. The resultant solution was extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:2 AcOEt:Hexane) to give cyclic carbamate **16a** (41.0 mg, 0.0834 mmol, 60% for 2 steps, 80% ee) as a white amorphous solid.

***tert*-Butyl 2-methoxy-2'-oxo-5-tosyloxy-2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (16a)**



$[\alpha]_D^{23}$ –82.8° (*c* 0.44, $CHCl_3$) for 80% ee. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.69 (2H, d, *J* = 8.5 Hz), 7.34 (2H, d, *J* = 8.5 Hz), 7.00 (1H, dd, *J* = 9.0, 2.4 Hz), 6.75 (1H, d, *J* = 9.0 Hz), 6.72 (1H, d, *J* = 2.4 Hz), 5.67 (1H, s), 5.01 (1H, d, *J* = 9.7 Hz), 3.92 (1H, d, *J* = 9.7 Hz), 3.66 (3H, s), 2.47 (3H, s), 1.28 (9H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 157.7, 151.6, 147.8, 145.9, 143.8, 132.1, 129.9, 128.6, 126.10, 126.07, 117.7, 111.2, 110.6, 85.2, 70.8, 66.9, 57.8, 27.6, 21.7. IR (neat, cm^{-1}): 3066, 3026, 2981, 2937, 2846, 1822, 1731, 1599. MS *m/z*: 491 (M^+), 391 (100%). HRMS (EI): Calcd. for $C_{23}H_{25}NO_9S$ (M^+): 491.1250, found: 491.1230. The enantiomeric excess of **16a** was determined to be 80% by chiral HPLC analysis using a CHIRALCEL OD-H (1:5 *i*-PrOH:Hexane, 0.5 mL/min): 33.4 min (minor enantiomer), 36.9 min (major enantiomer).

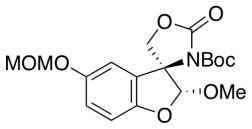
***tert*-Butyl 5-benzoyloxy-2-methoxy-2'-oxo -2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (16b)**



Purification: The crude **16b** was purified by silica gel column chromatography (1:4 to 1:2 AcOEt:Hexane) to give pure cyclic carbamate **16b** (70% for 2 steps, 78% ee) as a white solid.

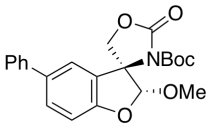
$[\alpha]_D^{24}$ –70.3° (*c* 0.94, $CHCl_3$) for 78% ee. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.19-8.14 (2H, m), 7.67-7.61 (1H, m), 7.55-7.48 (2H, m), 7.16 (1H, dd, *J* = 8.7, 2.4 Hz), 7.13 (1H, d, *J* = 2.4 Hz), 6.88 (1H, d, *J* = 8.7 Hz), 5.72 (1H, s), 5.11 (1H, d, *J* = 9.5 Hz), 4.17 (1H, d, *J* = 9.5 Hz), 3.69 (3H, s), 1.30 (9H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 165.3, 156.8, 152.0, 147.9, 145.4, 133.7, 130.1, 129.2, 128.6, 125.9, 124.9, 116.9, 111.0, 110.5, 85.2, 71.2, 67.1, 57.7, 27.5. IR (neat, cm^{-1}): 3066, 2980, 2939, 2848, 1822, 1736. MS *m/z*: 441 (M^+), 105 (100%). HRMS (EI): Calcd. for $C_{23}H_{23}NO_8$ (M^+): 441.1424, found: 441.1448. The enantiomeric excess of **16b** was determined to be 78% by chiral HPLC analysis using a CHIRALPAK IC (1:1 *i*-PrOH:Hexane, 0.5 mL/min): 28.3 min (minor enantiomer), 68.2 min (major enantiomer).

***tert*-Butyl 5-methoxymethoxy-2-methoxy-2'-oxo -2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (16c)**



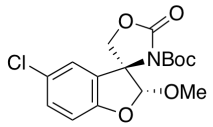
Purification: The crude **16c** was purified by silica gel column chromatography (1:4 to 1:2 AcOEt:Hexane) to give pure cyclic carbamate **16c** (50% for 2 steps, 73% ee) as a white solid. $[\alpha]_D^{25}$ –108.7° (*c* 0.41, $CHCl_3$) for 73% ee. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.00 (1H, dd, *J* = 8.7, 2.9 Hz), 6.94 (1H, d, *J* = 2.9 Hz), 6.75 (1H, d, *J* = 8.7 Hz), 5.66 (1H, s), 5.077 (1H, d, *J* = 9.5 Hz), 5.076 (2H, s), 4.13 (1H, d, *J* = 9.5 Hz), 3.66 (3H, s), 3.45 (3H, s), 1.25 (9H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 154.2, 152.5, 152.2, 148.1, 125.5, 120.3, 111.6, 111.0, 110.3, 95.5, 84.8, 71.5, 67.2, 57.6, 55.9, 27.5. IR (neat, cm^{-1}): 2978, 2936, 1822, 1732. MS *m/z*: 381 (M^+), 281 (100%). HRMS (EI): Calcd. for $C_{18}H_{23}NO_8$ (M^+): 381.1424, found: 381.1429. The enantiomeric excess of **16c** was determined to be 73% by chiral HPLC analysis using a CHIRALPAK IC (1:1 *i*-PrOH:Hexane, 0.5 mL/min): 28.6 min (minor enantiomer), 37.1 min (major enantiomer).

***tert*-Butyl 5-phenyl-2-methoxy-2'-oxo-2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (16d)**



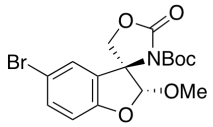
Purification: The crude **16d** was purified by silica gel column chromatography (1:6 to 1:4 AcOEt:Hexane) to give pure cyclic carbamate **16d** (88% for 2 steps, 75% ee) as a colorless oil. $[\alpha]_D^{28}$ –44.6° (*c* 1.29, $CHCl_3$) for 75% ee. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.56 (1H, dd, *J* = 8.8, 2.0 Hz), 7.51-7.47 (2H, m), 7.46-7.39 (3H, m), 7.36-7.30 (1H, m), 6.92 (1H, d, *J* = 8.8 Hz), 5.73 (1H, s), 5.12 (1H, d, *J* = 9.3 Hz), 4.21 (1H, d, *J* = 9.3 Hz), 3.70 (3H, s), 1.24 (9H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 158.7, 152.2, 148.0, 140.1, 135.6, 130.4, 128.9, 127.2, 126.7, 125.7, 121.8, 110.8, 110.3, 84.8, 71.2, 67.3, 57.7, 27.5. IR (neat, cm^{-1}): 3021, 2980, 2937, 2844, 1821, 1731, 1616. MS *m/z*: 397 (M^+), 297 (100%). HRMS (EI): Calcd. for $C_{22}H_{23}NO_6$ (M^+): 397.1525, found: 397.1532. The enantiomeric excess of **16d** was determined to be 75% by chiral HPLC analysis using a CHIRALPAK IA (1:10 *i*-PrOH:Hexane, 0.8 mL/min): 13.5 min (major enantiomer), 36.9 min (minor enantiomer).

***tert*-Butyl 5-chloro-2-methoxy-2'-oxo-2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (16e)**



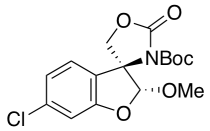
Purification: The crude **16e** was purified by silica gel column chromatography (1:6 to 1:4 AcOEt:Hexane) to give pure cyclic carbamate **16e** (65% for 2 steps, 89% ee) as a white solid. $[\alpha]_D^{26}$ –125.0° (*c* 0.93, $CHCl_3$) for 89% ee. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.28 (1H, dd, *J* = 8.3, 2.0 Hz), 7.23 (1H, d, *J* = 2.0 Hz), 6.79 (1H, d, *J* = 8.3 Hz), 5.69 (1H, s), 5.07 (1H, d, *J* = 9.6 Hz), 4.12 (1H, d, *J* = 9.6 Hz), 3.67 (3H, s), 1.28 (9H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 157.7, 151.7, 147.9, 131.4, 126.8, 126.5, 123.4, 111.7, 110.3, 85.1, 70.8, 67.0, 57.7, 27.5. IR (neat, cm^{-1}): 2980, 2938, 1825, 1731. MS *m/z*: 355 (M^+), 211 (100%). HRMS (EI): Calcd. for $C_{16}H_{18}ClNO_6$ (M^+): 355.0823, found: 355.0823. The enantiomeric excess of **16e** was determined to be 89% by chiral HPLC analysis using a CHIRALPAK AD-H (1:10 *i*-PrOH:Hexane, 0.8 mL/min): 17.9 min (major enantiomer), 32.2 min (minor enantiomer).

***tert*-Butyl 5-bromo-2-methoxy-2'-oxo -2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (16f)**



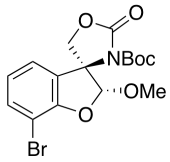
Purification: The crude **16f** was purified by silica gel column chromatography (1:6 to 1:2 AcOEt:Hexane) to give pure cyclic carbamate **16f** (50% for 2 steps, 84% ee) as a white solid. $[\alpha]_D^{24}$ –94.2° (*c* 0.72, $CHCl_3$) for 84% ee. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.42 (1H, dd, *J* = 8.4, 2.1 Hz), 7.36 (1H, d, *J* = 2.1 Hz), 6.74 (1H, d, *J* = 8.4 Hz), 5.68 (1H, s), 5.06 (1H, d, *J* = 9.5 Hz), 4.12 (1H, d, *J* = 9.5 Hz), 3.67 (3H, s), 1.28 (9H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 158.3, 151.7, 147.9, 134.3, 127.4, 126.3, 113.3, 112.3, 110.3, 85.2, 70.8, 67.1, 57.8, 27.6. IR (neat, cm^{-1}): 2980, 2937, 2848, 1824, 1731. MS *m/z*: 399 (M^+), 255 (100%). HRMS (EI): Calcd. for $C_{16}H_{18}BrNO_6$ (M^+): 399.0317, found: 399.0318. The enantiomeric excess of **16f** was determined to be 84% by chiral HPLC analysis using a CHIRALPAK IC (1:3 *i*-PrOH:Hexane, 0.5 mL/min): 36.9 min (minor enantiomer), 101.4 min (major enantiomer).

***tert*-Butyl 6-chloro-2-methoxy-2'-oxo-2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (16g)**



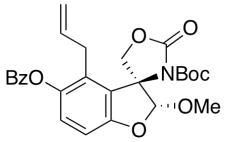
Purification: The crude **16g** was purified by silica gel column chromatography (1:4 to 1:2 AcOEt:Hexane) to give pure cyclic carbamate **16g** (61% for 2 steps, 92% ee) as a white solid. $[\alpha]_D^{31}$ –186.4° (*c* 0.59, $CHCl_3$) for 92% ee. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.16 (1H, d, *J* = 8.2 Hz), 6.99 (1H, dd, *J* = 8.2, 1.4 Hz), 6.87 (1H, dd, *J* = 8.2, 1.4 Hz), 5.70 (1H, s), 5.06 (1H, d, *J* = 9.7 Hz), 4.11 (1H, d, *J* = 9.7 Hz), 3.67 (3H, s), 1.28 (9H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 159.9, 151.8, 147.9, 137.0, 124.0, 123.8, 122.0, 111.3, 110.5, 85.0, 70.5, 67.0, 57.7, 27.5. IR (neat, cm^{-1}): 2982, 2943, 2848, 1824, 1731, 1608, 1599. MS *m/z*: 355 (M^+), 196 (100%). HRMS (EI): Calcd. for $C_{16}H_{18}ClNO_6$ (M^+): 355.0823, found: 355.0842. The enantiomeric excess of **16g** was determined to be 92% by chiral HPLC analysis using a CHIRALPAK IC (1:3 *i*-PrOH:Hexane, 0.5 mL/min): 29.4 min (minor enantiomer), 38.6 min (major enantiomer).

***tert*-Butyl 7-bromo-2-methoxy-2'-oxo-2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (16h)**



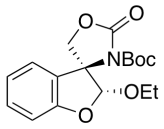
Purification: The crude **16h** was purified by silica gel column chromatography (1:6 to 1:2 AcOEt:Hexane) to give pure cyclic carbamate **16h** (26% for 2 steps, 85% ee) as a white solid. $[\alpha]_D^{24}$ –197.4° (*c* 0.82, $CHCl_3$) for 85% ee. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.49 (1H, dd, *J* = 7.8, 1.0 Hz), 7.19 (1H, dd, *J* = 7.8, 1.0 Hz), 6.90 (1H, dd, *J* = 7.8, 7.8 Hz), 5.74 (1H, s), 5.09 (1H, d, *J* = 9.7 Hz), 4.14 (1H, d, *J* = 9.7 Hz), 3.73 (3H, s), 1.24 (9H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 156.6, 151.9, 147.7, 134.4, 126.7, 123.0, 122.2, 110.0, 103.7, 85.1, 71.7, 67.1, 57.9, 27.5. IR (neat, cm^{-1}): 2980, 2941, 2850, 1825, 1728, 1605, 1589. MS *m/z*: 399 (M^+), 241 (100%). HRMS (EI): Calcd. for $C_{16}H_{18}BrNO_6$ (M^+): 399.0317, found: 399.0327. The enantiomeric excess of **16h** was determined to be 85% by chiral HPLC analysis using a CHIRALPAK IC (1:3 *i*-PrOH:Hexane, 0.5 mL/min): 42.3 min (minor enantiomer), 50.5 min (major enantiomer).

***tert*-Butyl 4-allyl-5-benzoyloxy-2-methoxy-2'-oxo-2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (16i)**



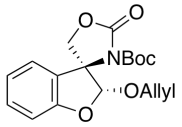
Purification: The crude **16i** was purified by silica gel column chromatography (1:4 AcOEt:Hexane) to give pure cyclic carbamate **16i** (61% for 2 steps, 51% ee) as a white amorphous solid.
$[\alpha]_D^{22}$ –43.1° (*c* 0.75, $CHCl_3$) for 51% ee. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.16 (2H, d, *J* = 7.7 Hz), 7.65 (1H, t, *J* = 7.7 Hz), 7.51 (2H, dd, *J* = 7.7, 7.7 Hz), 7.14 (1H, d, *J* = 8.7 Hz), 6.78 (1H, d, *J* = 8.7 Hz), 5.84 (1H, dddd, *J* = 17.4, 10.1, 5.8, 5.8 Hz), 5.67 (1H, s), 5.12 (1H, d, *J* = 9.7 Hz), 5.05-5.00 (1H, m), 4.95 (1H, d, *J* = 17.4 Hz), 4.29 (1H, d, *J* = 9.7 Hz), 3.69 (3H, s), 3.37-3.25 (2H, m), 1.31 (9H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 165.2, 156.8, 151.8, 147.9, 144.0, 133.8, 133.7, 130.1, 129.14, 129.11, 128.6, 125.6, 124.0, 117.0, 110.1, 109.1, 85.0, 71.6, 65.4, 57.8, 30.3, 27.5. IR (neat, cm^{-1}): 3076, 3013, 2981, 2937, 2846, 1822, 1735, 1601. MS *m/z*: 481 (M^+), 105 (100%). HRMS (EI): Calcd. for $C_{26}H_{27}NO_8$ (M^+): 481.1737, found: 481.1721. The enantiomeric excess of **16i** was determined to be 51% by chiral HPLC analysis using a CHIRALPAK IC (Mobile phase component A was Hexane, and mobile phase component B was *i*-PrOH. The linear gradient was: 0% B at 0 min, 0% B at 5 min, 50% B at 35 min, 50% B at 40 min, 0% B at 41 min, and 0% B at 45 min, at a flow rate of 1.0 mL/min.): 31.2 min (minor enantiomer), 33.1 min (major enantiomer).

***tert*-Butyl 2-ethoxy-2'-oxo-2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (15b)**



Purification: The crude **15b** was purified by silica gel column chromatography (1:4 AcOEt:Hexane) to give pure cyclic carbamate **15b** (47% for 2 steps, 61% ee) as a white solid.
$[\alpha]_D^{22}$ –119.4° (*c* 0.95, $CHCl_3$) for 61% ee. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.33-7.29 (1H, m), 7.24 (1H, dd, *J* = 7.8, 1.0 Hz), 6.99 (1H, ddd, 7.8, 7.8, 1.0), 6.83 (1H, d, *J* = 7.8 Hz), 5.77 (1H, s), 5.12 (1H, d, *J* = 9.8 Hz), 4.15 (1H, d, *J* = 9.8 Hz), 4.06 (1H, dq, *J* = 9.5, 7.5 Hz), 3.78 (1H, dq, *J* = 9.5, 7.5 Hz), 1.31 (3H, dd, *J* = 7.5, 7.5 Hz), 1.22 (9H, s). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 159.3, 152.3, 148.1, 131.4, 125.0, 123.3, 121.7, 110.6, 108.8, 84.7, 71.2, 67.5, 66.4, 27.5, 15.0. IR (neat, cm^{-1}): 2980, 2933, 1824, 1732, 1604. MS *m/z*: 335 (M^+), 162 (100%). HRMS (EI): Calcd. for $C_{17}H_{21}NO_6$ (M^+): 335.1369, found: 335.1398. The enantiomeric excess of **15b** was determined to be 61% by chiral HPLC analysis using a CHIRALPAK AD-H (1:5 *i*-PrOH:Hexane, 0.5 mL/min): 12.0 min (major enantiomer), 17.9 min (minor enantiomer).

***tert*-Butyl 2-(allyloxy)-2'-oxo-2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (15c)**



Purification: The crude **15c** was purified by silica gel column chromatography (1:6 AcOEt:Hexane) to give pure cyclic carbamate **15c** (37% for 2 steps, 55% ee) as a white solid.

$[\alpha]_D^{27}$ –116.2° (*c* 0.51, $CHCl_3$) for 55% ee. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.34-7.30 (1H, m), 7.25 (1H, dd, *J* = 7.8, 0.8 Hz), 7.02-6.98 (1H, m), 6.84 (1H, d, *J* = 8.0 Hz), 5.99-5.91 (1H, m), 5.81 (1H, s), 5.38-5.32 (1H, m), 5.30-5.26 (1H, m), 5.13 (1H, d, *J* = 9.3 Hz), 4.52-4.47 (1H, m), 4.31-4.25 (1H, m), 4.18 (1H, d, *J* = 9.3 Hz), 1.22 (9H, s). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 159.2, 152.2, 148.0, 132.7, 131.4, 125.0, 123.2, 121.8, 118.5, 110.6, 107.9, 84.7, 71.3, 70.9, 67.4, 27.4. IR (neat, cm^{-1}): 2981, 2936, 1823, 1732, 1604. MS *m/z*: 347 (M^+), 206 (100%). HRMS (EI): Calcd. for $C_{18}H_{21}NO_6$ (M^+): 347.1369, found: 347.1364. The enantiomeric excess of **15c** was determined to be 55% by chiral HPLC analysis using a CHIRALPAK AD-H (1:10 *i*-PrOH:Hexane, 0.5 mL/min): 17.9 min (major enantiomer), 27.6 min (minor enantiomer).

X-ray cryastallography

X-ray crystallographic file for **15a**:

Table 1. Crystal data and structure refinement for ydkr.

Identification code	ydkr	
Empirical formula	C16 H19 N O6	
Formula weight	321.32	
Temperature	173(2) K	
Wavelength	0.71075 Å	
Crystal system	?	
Space group	?	
Unit cell dimensions	a = 12.3682(4) Å	a= 90°.
	b = 8.2245(3) Å	b= 94.5114(12)°.
	c = 15.5806(6) Å	g = 90°.
Volume	1579.98(10) $Å^3$	
Z	4	
Density (calculated)	1.351 Mg/m^3	
Absorption coefficient	0.104 mm^{-1}	
F(000)	680	
Crystal size	0.40 x 0.40 x 0.30 mm^3	
Theta range for data collection	3.20 to 27.43°.	
Index ranges	-15<=h<=16, -9<=k<=10, -20<=l<=20	
Reflections collected	14406	
Independent reflections	3589 [R(int) = 0.0301]	
Completeness to theta = 27.43°	99.5 %	
Max. and min. transmission	0.9695 and 0.9596	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3589 / 0 / 212	
Goodness-of-fit on F^2	1.192	
Final R indices [I>2sigma(I)]	R1 = 0.0594, wR2 = 0.1351	
R indices (all data)	R1 = 0.0661, wR2 = 0.1462	
Largest diff. peak and hole	0.654 and -0.425 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for ydkr. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	5637(1)	5584(2)	8250(1)	26(1)
O(1)	4505(1)	5619(1)	7927(1)	33(1)
C(2)	3991(1)	4316(2)	8254(1)	29(1)
C(3)	2891(1)	4016(2)	8121(1)	39(1)
C(4)	2490(1)	2631(2)	8495(1)	45(1)
C(5)	3171(1)	1590(2)	8986(1)	42(1)
C(6)	4276(1)	1907(2)	9109(1)	34(1)
C(7)	4687(1)	3275(2)	8730(1)	26(1)
C(8)	5820(1)	3926(2)	8737(1)	24(1)
C(9)	6402(1)	4057(2)	9648(1)	32(1)
O(2)	7493(1)	3507(2)	9578(1)	39(1)
C(10)	7577(1)	2707(2)	8831(1)	30(1)
N(1)	6593(1)	2843(1)	8335(1)	24(1)
C(11)	6438(1)	2179(2)	7502(1)	23(1)
O(3)	5615(1)	2946(1)	7085(1)	27(1)
C(12)	5220(1)	2476(2)	6191(1)	28(1)
C(13)	4330(2)	3713(2)	5982(1)	42(1)
O(4)	5834(1)	6851(1)	8828(1)	35(1)
C(14)	5861(2)	8403(2)	8418(1)	49(1)
O(5)	8390(1)	2035(2)	8658(1)	43(1)
O(6)	6976(1)	1094(1)	7247(1)	31(1)
C(15)	4782(1)	752(2)	6198(1)	40(1)
C(16)	6129(1)	2687(2)	5599(1)	40(1)

Table 3. Bond lengths [Å] and angles [°] for ydkr.

C(1)-O(4)	1.3859(17)
C(1)-O(1)	1.4504(17)
C(1)-C(8)	1.5680(18)
C(1)-H(1)	1.0000
O(1)-C(2)	1.3650(18)
C(2)-C(3)	1.382(2)
C(2)-C(7)	1.386(2)
C(3)-C(4)	1.388(3)
C(3)-H(2)	0.9500
C(4)-C(5)	1.388(3)
C(4)-H(3)	0.9500
C(5)-C(6)	1.390(2)
C(5)-H(4)	0.9500
C(6)-C(7)	1.386(2)
C(6)-H(5)	0.9500
C(7)-C(8)	1.4993(19)
C(8)-N(1)	1.4809(17)
C(8)-C(9)	1.5443(18)
C(9)-O(2)	1.4361(18)
C(9)-H(6)	0.9900
C(9)-H(7)	0.9900
O(2)-C(10)	1.3492(18)
C(10)-O(5)	1.1958(18)
C(10)-N(1)	1.3937(17)
N(1)-C(11)	1.4080(17)
C(11)-O(6)	1.1994(17)
C(11)-O(3)	1.3228(16)
O(3)-C(12)	1.4906(16)
C(12)-C(13)	1.516(2)
C(12)-C(15)	1.518(2)
C(12)-C(16)	1.519(2)
C(13)-H(8)	0.9800
C(13)-H(9)	0.9800
C(13)-H(10)	0.9800

O(4)-C(14)	1.429(2)
C(14)-H(11)	0.9800
C(14)-H(12)	0.9800
C(14)-H(13)	0.9800
C(15)-H(14)	0.9800
C(15)-H(15)	0.9800
C(15)-H(16)	0.9800
C(16)-H(17)	0.9800
C(16)-H(18)	0.9800
C(16)-H(19)	0.9800

O(4)-C(1)-O(1)	109.05(11)
O(4)-C(1)-C(8)	109.17(11)
O(1)-C(1)-C(8)	106.47(11)
O(4)-C(1)-H(1)	110.7
O(1)-C(1)-H(1)	110.7
C(8)-C(1)-H(1)	110.7
C(2)-O(1)-C(1)	108.65(11)
O(1)-C(2)-C(3)	124.47(14)
O(1)-C(2)-C(7)	113.40(12)
C(3)-C(2)-C(7)	122.12(14)
C(2)-C(3)-C(4)	117.65(16)
C(2)-C(3)-H(2)	121.2
C(4)-C(3)-H(2)	121.2
C(3)-C(4)-C(5)	121.05(15)
C(3)-C(4)-H(3)	119.5
C(5)-C(4)-H(3)	119.5
C(4)-C(5)-C(6)	120.50(16)
C(4)-C(5)-H(4)	119.8
C(6)-C(5)-H(4)	119.8
C(7)-C(6)-C(5)	118.88(15)
C(7)-C(6)-H(5)	120.6
C(5)-C(6)-H(5)	120.6
C(6)-C(7)-C(2)	119.77(14)
C(6)-C(7)-C(8)	131.36(14)
C(2)-C(7)-C(8)	108.87(12)

N(1)-C(8)-C(7)	114.59(11)
N(1)-C(8)-C(9)	99.22(10)
C(7)-C(8)-C(9)	113.53(11)
N(1)-C(8)-C(1)	113.10(10)
C(7)-C(8)-C(1)	102.01(11)
C(9)-C(8)-C(1)	115.04(11)
O(2)-C(9)-C(8)	106.38(11)
O(2)-C(9)-H(6)	110.5
C(8)-C(9)-H(6)	110.5
O(2)-C(9)-H(7)	110.5
C(8)-C(9)-H(7)	110.5
H(6)-C(9)-H(7)	108.6
C(10)-O(2)-C(9)	110.80(11)
O(5)-C(10)-O(2)	122.88(13)
O(5)-C(10)-N(1)	128.69(14)
O(2)-C(10)-N(1)	108.42(12)
C(10)-N(1)-C(11)	121.96(11)
C(10)-N(1)-C(8)	112.30(11)
C(11)-N(1)-C(8)	125.25(11)
O(6)-C(11)-O(3)	128.16(12)
O(6)-C(11)-N(1)	123.67(12)
O(3)-C(11)-N(1)	108.17(11)
C(11)-O(3)-C(12)	121.21(10)
O(3)-C(12)-C(13)	101.85(11)
O(3)-C(12)-C(15)	109.02(12)
C(13)-C(12)-C(15)	111.98(14)
O(3)-C(12)-C(16)	109.50(12)
C(13)-C(12)-C(16)	110.71(14)
C(15)-C(12)-C(16)	113.17(14)
C(12)-C(13)-H(8)	109.5
C(12)-C(13)-H(9)	109.5
H(8)-C(13)-H(9)	109.5
C(12)-C(13)-H(10)	109.5
H(8)-C(13)-H(10)	109.5
H(9)-C(13)-H(10)	109.5
C(1)-O(4)-C(14)	112.96(12)

O(4)-C(14)-H(11)	109.5
O(4)-C(14)-H(12)	109.5
H(11)-C(14)-H(12)	109.5
O(4)-C(14)-H(13)	109.5
H(11)-C(14)-H(13)	109.5
H(12)-C(14)-H(13)	109.5
C(12)-C(15)-H(14)	109.5
C(12)-C(15)-H(15)	109.5
H(14)-C(15)-H(15)	109.5
C(12)-C(15)-H(16)	109.5
H(14)-C(15)-H(16)	109.5
H(15)-C(15)-H(16)	109.5
C(12)-C(16)-H(17)	109.5
C(12)-C(16)-H(18)	109.5
H(17)-C(16)-H(18)	109.5
C(12)-C(16)-H(19)	109.5
H(17)-C(16)-H(19)	109.5
H(18)-C(16)-H(19)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for ydkr. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	28(1)	24(1)	26(1)	-1(1)	4(1)	2(1)
O(1)	27(1)	34(1)	37(1)	8(1)	1(1)	5(1)
C(2)	29(1)	33(1)	25(1)	-2(1)	6(1)	2(1)
C(3)	26(1)	55(1)	36(1)	-2(1)	3(1)	4(1)
C(4)	30(1)	61(1)	44(1)	-10(1)	11(1)	-10(1)
C(5)	42(1)	42(1)	46(1)	-4(1)	17(1)	-13(1)
C(6)	39(1)	31(1)	33(1)	0(1)	10(1)	-1(1)
C(7)	27(1)	28(1)	23(1)	-4(1)	6(1)	1(1)
C(8)	26(1)	25(1)	20(1)	-1(1)	3(1)	2(1)
C(9)	35(1)	37(1)	22(1)	-2(1)	0(1)	5(1)
O(2)	33(1)	53(1)	28(1)	-7(1)	-8(1)	10(1)
C(10)	29(1)	34(1)	26(1)	1(1)	-4(1)	5(1)
N(1)	23(1)	26(1)	22(1)	-1(1)	1(1)	4(1)
C(11)	22(1)	24(1)	23(1)	1(1)	3(1)	-1(1)
O(3)	29(1)	31(1)	20(1)	-4(1)	-2(1)	7(1)
C(12)	32(1)	32(1)	19(1)	-4(1)	-2(1)	2(1)
C(13)	45(1)	49(1)	30(1)	-4(1)	-10(1)	15(1)
O(4)	48(1)	25(1)	33(1)	-4(1)	6(1)	0(1)
C(14)	72(1)	23(1)	52(1)	-1(1)	11(1)	2(1)
O(5)	30(1)	58(1)	39(1)	-5(1)	-5(1)	16(1)
O(6)	30(1)	30(1)	31(1)	-5(1)	3(1)	7(1)
C(15)	42(1)	38(1)	40(1)	-4(1)	-5(1)	-9(1)
C(16)	47(1)	47(1)	26(1)	2(1)	8(1)	1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for ydkr.

	x	y	z	U(eq)
H(1)	6119	5669	7766	31
H(2)	2426	4731	7786	47
H(3)	1738	2392	8412	54
H(4)	2879	654	9241	51
H(5)	4742	1199	9448	41
H(6)	6399	5196	9853	38
H(7)	6035	3368	10058	38
H(8)	3755	3563	6373	63
H(9)	4029	3563	5387	63
H(10)	4630	4812	6052	63
H(11)	6336	8350	7944	73
H(12)	6139	9219	8837	73
H(13)	5127	8705	8191	73
H(14)	5386	-14	6297	60
H(15)	4385	515	5643	60
H(16)	4292	643	6659	60
H(17)	6448	3772	5682	59
H(18)	5839	2563	4999	59
H(19)	6688	1861	5735	59

Table 6. Torsion angles [°] for ydkr.

O(4)-C(1)-O(1)-C(2)	-109.96(12)
C(8)-C(1)-O(1)-C(2)	7.71(14)
C(1)-O(1)-C(2)-C(3)	176.12(14)
C(1)-O(1)-C(2)-C(7)	-5.13(16)
O(1)-C(2)-C(3)-C(4)	179.66(14)
C(7)-C(2)-C(3)-C(4)	1.0(2)
C(2)-C(3)-C(4)-C(5)	0.2(3)
C(3)-C(4)-C(5)-C(6)	-0.6(3)
C(4)-C(5)-C(6)-C(7)	-0.3(2)
C(5)-C(6)-C(7)-C(2)	1.5(2)
C(5)-C(6)-C(7)-C(8)	-179.48(14)
O(1)-C(2)-C(7)-C(6)	179.30(12)
C(3)-C(2)-C(7)-C(6)	-1.9(2)
O(1)-C(2)-C(7)-C(8)	0.10(16)
C(3)-C(2)-C(7)-C(8)	178.87(13)
C(6)-C(7)-C(8)-N(1)	62.80(19)
C(2)-C(7)-C(8)-N(1)	-118.12(12)
C(6)-C(7)-C(8)-C(9)	-50.2(2)
C(2)-C(7)-C(8)-C(9)	128.83(13)
C(6)-C(7)-C(8)-C(1)	-174.62(14)
C(2)-C(7)-C(8)-C(1)	4.46(14)
O(4)-C(1)-C(8)-N(1)	-126.06(12)
O(1)-C(1)-C(8)-N(1)	116.35(12)
O(4)-C(1)-C(8)-C(7)	110.34(12)
O(1)-C(1)-C(8)-C(7)	-7.25(13)
O(4)-C(1)-C(8)-C(9)	-13.02(16)
O(1)-C(1)-C(8)-C(9)	-130.61(12)
N(1)-C(8)-C(9)-O(2)	16.37(14)
C(7)-C(8)-C(9)-O(2)	138.42(13)
C(1)-C(8)-C(9)-O(2)	-104.58(13)
C(8)-C(9)-O(2)-C(10)	-15.05(17)
C(9)-O(2)-C(10)-O(5)	-174.39(15)
C(9)-O(2)-C(10)-N(1)	6.45(17)
O(5)-C(10)-N(1)-C(11)	-1.3(2)

O(2)-C(10)-N(1)-C(11)	177.76(12)
O(5)-C(10)-N(1)-C(8)	-173.71(16)
O(2)-C(10)-N(1)-C(8)	5.39(16)
C(7)-C(8)-N(1)-C(10)	-134.76(12)
C(9)-C(8)-N(1)-C(10)	-13.48(14)
C(1)-C(8)-N(1)-C(10)	108.88(13)
C(7)-C(8)-N(1)-C(11)	53.17(17)
C(9)-C(8)-N(1)-C(11)	174.45(12)
C(1)-C(8)-N(1)-C(11)	-63.19(16)
C(10)-N(1)-C(11)-O(6)	22.2(2)
C(8)-N(1)-C(11)-O(6)	-166.48(13)
C(10)-N(1)-C(11)-O(3)	-158.43(12)
C(8)-N(1)-C(11)-O(3)	12.92(17)
O(6)-C(11)-O(3)-C(12)	1.7(2)
N(1)-C(11)-O(3)-C(12)	-177.65(11)
C(11)-O(3)-C(12)-C(13)	-177.65(13)
C(11)-O(3)-C(12)-C(15)	63.87(16)
C(11)-O(3)-C(12)-C(16)	-60.43(17)
O(1)-C(1)-O(4)-C(14)	-73.72(16)
C(8)-C(1)-O(4)-C(14)	170.32(13)

Symmetry transformations used to generate equivalent atoms:

VCD spectroscopy and computation

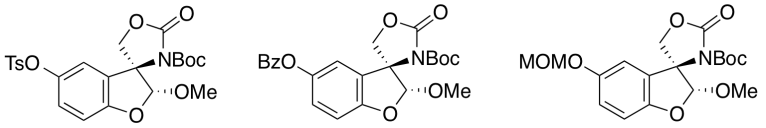
VCD

VCD and IR spectra were measured on a BioTools Chiralir spectrometer equipped with a second photoelastic modulator. Spectra were recorded in $CDCl_3$ using a 100 μm CaF_2 cell at a resolution of 8 cm^{-1} at ambient temperature. All spectral data were corrected by a solvent spectrum obtained under the same experimental condition, and presented as Δε and ε (both in $M^{-1}cm^{-1}$).

Computation

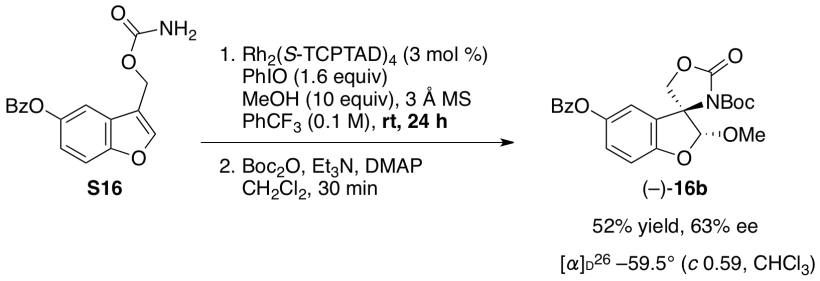
Geometry optimizations and spectral calculations were carried out on Gaussian 03 package.[11] All calculation was conducted without considering solvent effects. Prior to the calculation of vibrational spectra of the spirocycle **15a**, a conformational search was performed for (2*R*,3*S*)-**15a** to define its stable conformers. Various conformers that differ in the orientation of the 3-OMe and NBoc groups as well as the puckering of the five membered rings were manually generated, and each geometry was optimized by using the DFT/B3LYP/6-311G(d,p) level of theory. The resulting conformers within a 2 kcal/mol window were further optimized at the DFT/B3LYP/6-311+G(d,p) level of theory, which yielded three stable conformers. Their IR and VCD spectra were calculated at the DFT/B3LYP/6-311+G(d,p) level, and simulated with Lorentzian lineshapes of 8 cm^{-1} width. The calculated frequencies ν were scaled with the equation of $0.9894\nu - 0.0000104\nu^2$. Final spectra were obtained based on the Boltzmann population average of each spectrum.

Determination of the absolute configurations of (–)-16a, (–)-16b, and (–)-16c

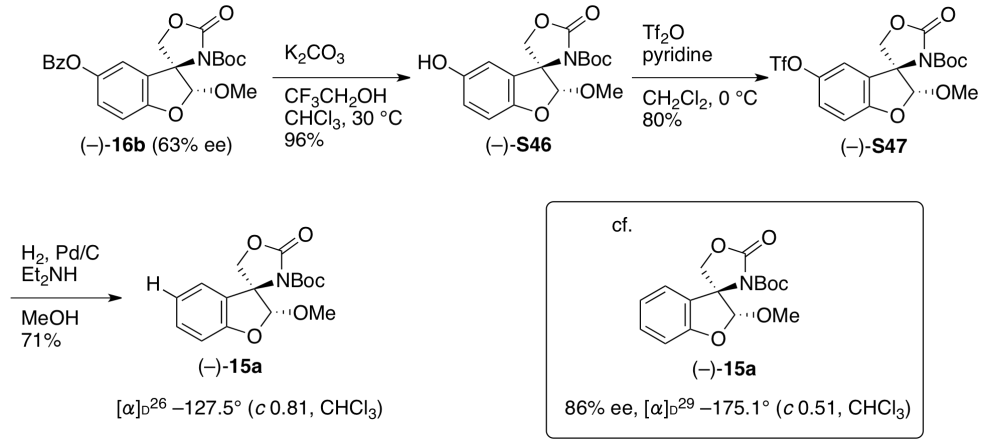


The relative stereostructures of (–)-**16a**, (–)-**16b**, and (–)-**16c** were established by chemical transformation and comparing the ^{1}H-NMR. The absolute stereostructures of (–)-**16a**, (–)-**16b**, and (–)-**16c** were established by chemical transformation and comparing the optical rotation (Scheme S11 and S12).

Scheme S11: Determination of the absolute configuration of spirocycle (–)-16b

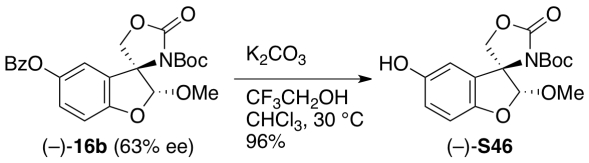


cf. The spirocycle (–)-**16b** (63% ee) was used in this section.



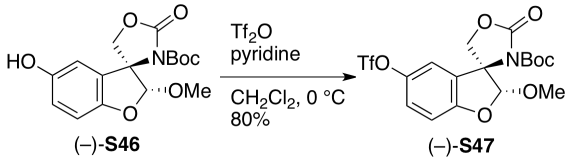
cf. Hydrodeoxygenation of phenol triflate (–)-**S47**, see: ref. (12).

The relative configuration of **(–)-16b** was determined as shown in Scheme S11 by comparing the ^{1}H-NMR of above synthesized **15a** with the ^{1}H-NMR of (–)-**15a** which was prepared by asymmetric aza-spiroannulation of benzofuran **8**. The absolute configuration was also determined by comparing the sign of the optical rotation (The absolute stereochemistry of spirocycle (–)-**15a**, which was prepared by asymmetric aza-spiroannulation, has already been determined by VCD spectroscopy: see Figure S1). As a result, the absolute stereostructure of (–)-**16b** was elucidated to be (2*R*,3*S*).



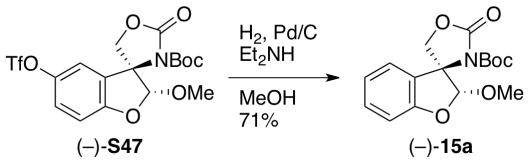
***tert*-Butyl 5-hydroxy-2-methoxy-2'-oxo -2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (S46)**: To a solution of cyclic carbamate **16b** (102 mg, 0.231 mmol) in CF_3CH_2OH (2.3 mL) and $CHCl_3$ (2.3 mL) was added K_2CO_3 (32 mg, 0.231 mmol) at room temperature. The resulting solution was stirred at 30 °C for 14 h. After cooling to room temperature, the resultant solution was added saturated aqueous NH_4Cl, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 to 1:1 AcOEt:Hexane) to give phenol **S46** (75 mg, 0.222 mmol, 96%) as a white amorphous solid.

$[\alpha]_D^{24}$ –97.2° (*c* 0. 14, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.81 (1H, dd, *J* = 8.6, 2.6 Hz), 6.75 (1H, d, *J* = 2.6 Hz), 6.70 (1H, d, *J* = 8.6 Hz), 5.65 (1H, s), 5.21 (1H, br s), 5.07 (1H, d, *J* = 9.6 Hz), 4.13 (1H, d, *J* = 9.6 Hz), 3.65 (3H, s), 1.27 (9H, s). ^{13}C-NMR (150 MHz, $CDCl_3$): δ 153.1, 152.3, 150.8, 148.1, 125.6, 118.5, 111.0, 110.1, 109.9, 85.0, 71.6, 67.3, 57.6, 27.6. IR (neat, cm^{-1}): 3437, 2981, 2937, 2840, 1813, 1734. MS *m/z*: 337 (M^+), 237 (100%). HRMS (EI): Calcd. for $C_{16}H_{19}NO_7$: 337.1162, found: 337.1146.



***tert*-Butyl 5-trifluoromethansulfonyloxy-2-methoxy-2'-oxo -2*H*-spiro[benzofuran-3,4'-oxazolidine]-3'-carboxylate (S47)**: To a solution of phenol **S46** (39.0 mg, 0.116 mmol) in CH_2Cl_2 (1.2 mL) were added Tf_2O (25 μL, 0.151 mmol) and pyridine (56μL, 0.696 mmol) at 0 °C, and stirred for 15 min. The resultant solution was added saturated aqueous $NaHCO_3$, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 AcOEt:Hexane) to give triflate **S47** (43.8 mg, 0.0933 mmol, 80%) as a white solid.

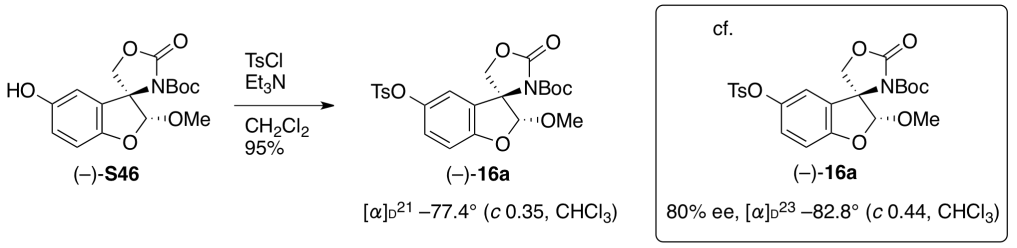
$[\alpha]_D^{23}$ –79.0° (*c* 0.86, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.24 (1H, dd, *J* = 8.7, 2.6 Hz), 7.18 (1H, d, *J* = 2.6 Hz), 6.90 (1H, d, *J* = 8.7 Hz), 5.74 (1H, s), 5.11 (1H, d, *J* = 9.5 Hz), 4.11 (1H, d, *J* = 9.5 Hz), 3.70 (3H, s), 1.28 (9H, s). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 158.6, 151.5, 147.7, 143.5, 127.0, 124.7, 118.7 (q, *J* = 322.4 Hz), 117.0, 111.6, 110.8, 85.4, 70.7, 66.8, 57.9, 27.4. IR (neat, cm^{-1}): 2983, 2940, 2850, 1826, 1732. MS *m/z*: 469 (M^+), 192 (100%). HRMS (EI): Calcd. for $C_{17}H_{18}F_3NO_9S$: 469.0654, found: 469.0667.



(–)-**S47** (–)-**15a**

After two vacuum/H_2 cycles to replace air inside the reaction flask with hydrogen, a mixture of the triflate **S47** (39.0 mg, 0.0830 mmol), 10% Pd/C (3.9 mg, 10 wt% of **S47**), and Et_2NH (13 μL, 0.125 mmol) in MeOH (1.7 mL) was vigorously stirred at room temperature under an ordinary hydrogen pressure (balloon) for 18 h. The reaction mixture was filtered through a Celite pad, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 to 1:2 AcOEt:Hexane) to give cyclic carbamate **15a** (19.0 mg, 0.0591 mmol, 71%) as a white solid.

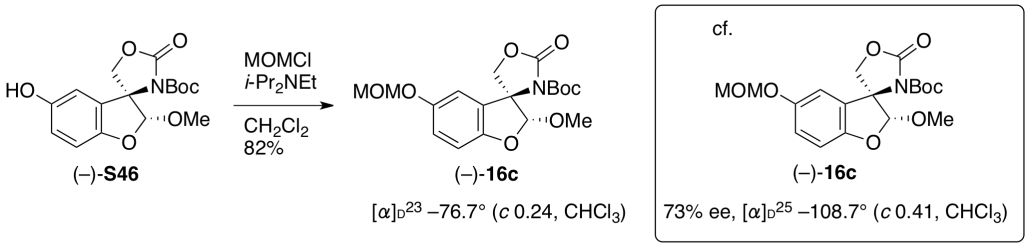
Scheme S12: Determination of absolute configurations of spirocycles (–)-16a and (–)-16c



(–)-**S46** (–)-**16a** (–)-**16a**

$[\alpha]_D^{21}$ –77.4° (*c* 0.35, $CHCl_3$) 80% ee, $[\alpha]_D^{23}$ –82.8° (*c* 0.44, $CHCl_3$)

(–)-**S46**: prepared from **16b** (63% ee),
absolute stereostructure has already been determined as shown here: see Scheme S11

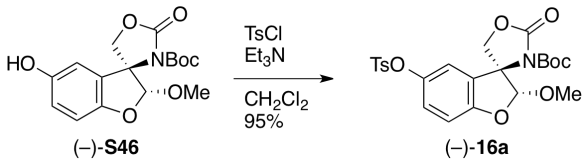


(–)-**S46** (–)-**16c** (–)-**16c**

$[\alpha]_D^{23}$ –76.7° (*c* 0.24, $CHCl_3$) 73% ee, $[\alpha]_D^{25}$ –108.7° (*c* 0.41, $CHCl_3$)

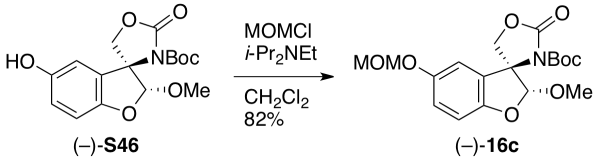
(–)-**S46**: prepared from **16b** (63% ee),
absolute stereostructure has already been determined as shown here: see Scheme S11

The relative configurations of (–)-**16a** and (–)-**16c** was determined as shown in Scheme S12 by comparing the ^{1}H-NMR of above synthesized **16a** and **16c** with the ^{1}H-NMR of (–)-**16a** and (–)-**16c** which were prepared by asymmetric aza-spiroannulation of benzofurans **S14** and **S18** respectively. The absolute configurations were also determined by comparing the sign of the optical rotation. As a result, the absolute stereostructures of (–)-**16a** and (–)-**16c** were elucidated to be (2*R*,3*S*).



(–)-**S46** (–)-**16a**

To a solution of phenol **S46** (5.0 mg, 0.0148 mmol) in CH_2Cl_2 (0.3 mL) were added TsCl (3.70 mg, 0.0192 mmol) and Et_3N (5.4 μL, 0.0385 mmol) at 0 °C. The mixture was allowed to warm to room temperature, and stirred for 1 h. The resultant solution was added water, and extracted with AcOEt. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 to 1:2 AcOEt:Hexane) to give tosylate **16a** (6.9 mg, 0.0140 mmol, 95%) as a white solid.



(–)-**S46** (–)-**16c**

To a solution of phenol **S46** (5.0 mg, 0.0148 mmol) in CH_2Cl_2 (0.3 mL) were added MOMCl (6.6 μL, 0.0888 mmol) and *i*-Pr_2NEt (25 μL, 0.148 mmol) at 0 °C. The mixture was allowed to warm to room temperature, and stirred for 12 h. The resultant solution was added saturated aqueous $NaHCO_3$, and extracted with Et_2O. The combined extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (1:4 to 1:1 AcOEt:Hexane) to give MOM-ether **16c** (4.6 mg, 0.0121 mmol, 82%) as a white solid.

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